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VOLUME II

THE CLINICAL DIAGNOSIS OF INTERNAL DISEASES

BY

LEWELLYS F. BARKER, M.D. (Tor.), LL.D. (Queens; McGill

PROFESSOR OF MEDICINE, JOHNS HOPKINS UNIVERSITY, 1905–1914; PHYSICIAN-IN-CHIEF, JOHNS HOPKINS HOSPITAL, 1905–1914; PRESIDENT OF ASSOCIATION OF AMERICAN PHYSICIANS, 1912–1913; PRESIDENT OF AMERICAN NEUROLOGICAL ASSOCIATION, 1915; PRESIDENT OF NATIONAL COMMITTEE FOR MENTAL HYGIENE; PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY; AND VISITING PHYSICIAN, JOHNS HOPKINS HOSPITAL

WITH TEN COLORED PLATES AND TWO HUNDRED AND NINETY ILLUSTRATIONS IN TEXT

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THE CLINICAL DIAGNOSIS OF INTERNAL DISEASES

GENERAL DIAGNOSIS, INFECTIONS, RESPIRATORY AND CIRCULATORY SYSTEMS

BY

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PROFESSOR OF MEDICINE, JOHNS HOPKINS UNIVERSITY, 1905–1914; PHYSICIAN-IN-CHIEF, JOHNS HOPKINS HOSPITAL, 1905–1914; PRESIDENT OF ASSOCIATION OF AMERICAN PHYSICIANS, 1912–1913; PRESIDENT OF AMERICAN NEUROLOGICAL ASSOCIATION, 1915; PRESIDENT OF NATIONAL COMMITTEE FOR MENTAL HYGIENE; PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY; AND VISITING PHYSICIAN, JOHNS HOPKINS HOSPITAL

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Preface

In view of the enormous advances made in the sciences formerly termed auxiliary to medicine, but now recognized as fundamental for all progress in the healing art, the time would seem ripe for a publication dealing in a simple, practical way with the clinical diagnosis of internal diseases.

In the last decade the viewpoint of internists has to a certain extent been shifted, in that they are now attempting to visualize clearly the functional pathological processes that are the essence of disease. They are studying, too, the causes—external and internal—of the deviations from the normal met with in disease; and they are no longer content merely with setting up clinical syndromes, or with attempting to prophesy, during life, the anatomical lesions that pathologists will find in the bodies of their patients after death. Control of clinical work by the methods of pathological anatomy and histology will always be highly desirable; but for the clinical diagnosis of internal diseases today, a knowledge of functional pathology and of its underlying sciences (biophysics and biochemistry) is quite as important as a knowledge of pathological anatomy. Indeed, this substitution of the viewpoint of functional pathology for that of structural pathology in discussions of the principles and in determining the practice of inner medicine represents the most radical departure in our science since Virchow so profoundly influenced it by the introduction of the conceptions of cellular pathology over fifty years ago.

The growth of the sciences underlying clinical work has been so rapid and the progress so great that an inner medicine can now be constructed that is very different in form, methods, and emphasis from the inner medicine of any previous period—so different, indeed, that of the men trained in the art and science of diagnosis a few years ago, only those that have had exceptional opportunities for keeping pace with changes can find their way in it without a special guide. To provide such an everyday guide for practitioners, and for students who are now entering upon the study of clinical medicine, this work has been planned and written. In it an attempt has been made to present in due proportion the methods and results of the science of medical diagnosis, in all its parts. The work has been written from the viewpoint of functional pathology, as far as this is possible at the present time, but the results of etiological and pathological-anatomical studies have been also regarded.

With our present knowledge, *diagnosis* should mean not the mere placing of a patient's malady in a particular group and the assignment to it of a name, but rather a thorough knowledge of the patient and the arrival at an understanding of the essence of those deviations from normal functions that the patient presents. Thus understood, diagnosis involves (1) the accumulation of data by all possible methods (physical, chemical, biological, psychical, social, experimental) that can yield information of importance regarding the patient's body and mind; (2) the drawing of whatever inferences are justifiable therefrom. To make such a diagnosis requires much knowledge of both bedside methods of examination and laboratory technic, and skill acquired by practice in the use of them.

Clinical men have come to realize that they cannot expect the laboratory workers in the non-clinical medical sciences to solve clinical problems for them, for these men have the problems of their own sciences to solve, and the application of the scientific facts discovered by them, in so far as they offer a solution of diagnostic and therapeutic difficulties, must be made by the clinicians themselves. Technical application always involves new investigations, which fortunately often not only contribute to the progress of clinical medicine itself but also advance the sciences underlying it.

It may be asked whether the present state of inner medicine really justifies an attempt at description from the viewpoint of functional pathology. That such a presentation is not easy, and that it must fall far short of what one would like it to be, must at once be admitted. Certain parts only of inner medicine have been well worked up on the functional pathological side; others are as yet almost wholly unexplored. At the present time, when there is a seething activity in our clinics in the application of biochemical and biophysical methods to diagnosis, it can scarcely fail to be helpful to patients and physicians, to teachers and students, and even to original investigators, to take stock of what has already been accomplished, to point out the gaps in our knowledge, and to indicate unknown fields that may most profitably be explored. For nothing, perhaps, contributes more to the further progress of an unevenly developed subject than a clear and concise presentation of its state at a given time; the practical value of the results obtained in well-tilled districts serves as a spur to the cultivation of unbroken ground. A survey of inner medicine in the light of functional pathology is not only justifiable at this moment but, for the welfare of our profession, is urgently demanded.

Naturally it might be asked: Should any one man, in a time like ours, try to write a textbook of clinical diagnosis that covers the whole field of inner medicine and its specialties? Is it not essential that such a work be written by a large group of specialists, each one contributing the chapter bearing upon the particular domain in which he is an expert?

The writer has considered this question very seriously before deciding to stand as single sponsor for the present work. All will agree that in the preparation of large systematic treatises, it is desirable that the single parts be written by special investigators in the several domains. For the time has long since passed when any one man can be equally interested, active, and productive in all parts of inner medicine. Each of the medical specialties requires for its mastery so much experimental work, so much technical skill, and such a wealth of detail and depth of special knowledge, that a firm grasp of more than one or two specialties exceeds the power of a single person. In large treatises, furthermore, it is not permissible to omit even less important details; the specialist is required to discuss theories at length, even those that are of uncertain value. But the writing of a monograph is an entirely different problem. In it, there must be a careful selection, a separation of the relatively important from the less important, the avoidance of unnecessary ballast, and compression within set limits. Hence it would seem desirable that a monograph on the diagnosis of internal diseases be produced by a single writer, provided this writer has had large clinical opportunities, some years of laboratory training, and has been in close contact with original workers in the several specialties, always moreover provided that he has good judgment regarding the needs of students and general practitioners, a wide acquaintance with home and foreign literature, and the kind of mind that permits him to sift critically, to balance evenly, to write concisely and to express himself clearly; for such a practical diagnostician, imbued with the scientific spirit, should be able to prepare a valuable clinical work if the purpose for which it is designed be kept plainly in view during its production. To a full possession of the ideal qualifications just enumerated the author makes no claim. None can feel more keenly the shortcomings of the present work. Should it, however, be adjudged to have met, to some extent, an existing need, it is hoped that other teachers and practitioners may be kind enough to call attention to mistakes and omissions, so that their coöperation will render possible a more adequate presentation of the subject at a later period. There is one best way to do everything, and the sooner the "standard methods" are found and adopted, everywhere, by single workers, the greater will be their efficiency.

In the arrangement and presentation of this material, the practical needs of students and of physicians have been kept foremost in mind. The idea underlying the plan has been to write the work in such a way that any one using it, no matter what his special training, will find in it directions that will, if consistently followed, permit him to make a complete examination of all parts of the human body by both the clinical and the laboratory methods now in use, and to draw from the data thus accumulated all justifiable inferences. The

to lay equal stress upon all the branches of inner medi-
long-winded discussions and the inclusion of unimportant
as that that is as uncertain and debatable. The infor-
believed to be full enough to permit a clinician to work
lowing the text, thus avoiding the necessity and trouble of
series of special treatises in everyday work. To preserve,
compendious character of the treatise, it has not been thought
include all the thousand and one methods that are available,
in detail, the advantages and disadvantages of those that
The student or practitioner who on occasion may desire
ation than is here given, or may require to use, for some
h, methods not sufficiently practical to justify their inclu-
ork, will find appended to the several sections bibliographic
which the additional information may be found. In select-
erences I have been influenced by (1) the historical impor-
articles, (2) American work, and (3) the recency of the
It will be noticed that a number of methods usually found
of diagnosis are missing; on careful consideration, methods
been judged to be antiquated or that have been perpetuated by
piety, have been omitted. Additional brevity in the text
made possible by the introduction of many explanatory charts,
trations.

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in gaining the experience upon which the work is pri-
and in the preparation and arrangement of the abundant
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In conclusion, it may be mentioned that the writing of this monograph was begun before the outbreak of the great world war. It was the desire of the author from the beginning, while attempting adequately to present the results of American work, to value properly, also, the researches of clinicians in all countries. Since the outbreak of the war the writing has been continued precisely in the spirit in which it was begun, and in the bibliography cited every effort has been made to avoid any one-sided or prejudiced consideration of the literature. Medicine is not a national subject; it is and must ever continue to be an international science. Every physician who has the real progress of medicine at heart should at all times, and despite all, see to it that he does all in his power to keep the bonds of scientific brotherhood unbroken.

LEWELLYS F. BARKER.

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Part I

General Plan for the Clinical Study of a Patient

A. Introduction

In no part of medicine has greater progress been made during the st decade than in clinical diagnosis. The careful control of clinical udies at the end of the nineteenth century by means of pathological natomy and histology prepared the way for what we are now witnessing, amely, a great development of internal medicine as influenced by patho-gical physiology. The application of physical, chemical and biological ethods to the study of disease during life is what chiefly characterizes edicine at the beginning of the twentieth century.

There is such a wealth of new methods and the data that can be cumulated regarding a single patient are so numerous, that one who gins to work in internal medicine, unless carefully and judiciously led, ay easily become confused and find difficulty in deciding what is rel-tively important and what relatively unimportant in a given instance. n experienced clinician gradually learns to select from the multitude f phenomena presented to him in a given case the characteristic and ssential features of that higher reality, a "clinical picture," much as an rtist on viewing nature selects and combines, for his purposes, the ele-ents necessary for his work of art.

The science and art of internal medicine are always leading to the construction f new clinical pictures. A student is fortunate when, in his early work, he is privileged to observe the clinical pictures constructed by masters of internal medicine, either as demonstrated to him as living patients, or as vividly reported for him so that he may visualize the picture by reading the records of observation left by such masters. But there is no royal road to clinical knowledge and experience; the novice must learn the technic of the clinical art, beginning with the simplest methods of analysis, practicing one method after another, at the bedside and in the laboratory, and continuing his practice under instruction, until he attains to skill. He must not expect in his earlier analytical studies to be able to judge of the proportionate value of the individual data obtained by analysis. Only after considerable experience dare he hope to be able properly to synthesize the data

and to compose a clinical picture in which the interest will center in the n portant facts, with all the accessory facts duly subordinated. Native capa clinical work is essential to the highest success. In the study of pictorial ar everyone can learn to paint pictures by long study and training, but not e can become a Velasquez; similarly, any person of average intelligence ca the technic of studying patients, but it is not given to many to compose pictures as did Sydenham and Graves, or Laennec and Trousseau, or Fr and Kussmaul, or Flint, Janeway, and Fitz, to mention only some of the internists no longer living.

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Many other journals, American and foreign, will be referred to in the individual references throughout the book. For the bibliography of modern medicine the student should consult the Index Catalogue of the Library of the Surgeon-General's Office (34 vols., 1879–1913), supplemented by the monthly "Index Medicus" (1879–1899; 1903–1915).

B. The Clinical History

In collecting the clinical data, preceding their synthesis to a "clinical picture," in an individual case, it is desirable to follow some more or less systematic plan, for otherwise important points may easily be overlooked. The results of the clinical analysis are recorded in a so-called *Clinical History.*

The clinical history consists of four parts: (1) the anamnesis, (2) the status praesens, (3) the catamnesis, and (4) the epicrisis.

1. **Anamnesis.**—This is the account given by the patient and his friends of the life of the patient previous to the time of examination.

2. **Status praesens.**—This is the record of the objective examination of the patient by the physician, with the aid of physical, chemical, and biological (including psychological) methods.

3. **Catamnesis.**—This is the subsequent history of the patient, including notes on the course of the disease, the kind of treatment used, and the results thereof.

4. **Epicrisis.**—This is the physician's final judgment upon the case, with discussion of all the findings. It is especially valuable for science in instances in which the clinical history has been controlled by surgical operation, or, in case of death, by autopsy.

1. The Anamnesis

The taking of a proper anamnesis is not easy. It requires, if it is to be well taken, a large experience, and a wide familiarity with the phenomena of disease; in the absence of these, it is scarcely possible, by inquiry, to obtain a correct idea of the previous history of the disease, and of the subjective symptoms from which the patient suffers. An experienced clinician insists, when possible, on taking the anamnesis himself, especially in obscure cases. He can much more safely delegate the making of a physical examination to a less experienced man, than deprive him-

self of the knowledge gained through personally obtaining the anamnestic data.

Here, as everywhere, however, one has to learn by *doing*, and in acquiring skill it is well, at any rate for beginners, to follow a definite plan, asking certain questions, in every case, in serial sequence. Later on, it may be permissible to take "short cuts." An experienced consultant will sometimes secure a better anamnesis in five or ten minutes than the fourth year student can secure in an hour, but the briefer route dare not be followed by the tyro. And even the most skillful and experienced will overlook important items if he deviate too far from a well-ordered plan, or remain satisfied with too brief a questionaire.

In taking the anamnesis, the physician tries to get as exact a description of the abnormal sensations and feelings of the patient as possible, their duration, and the order in which they appeared. In recording these, it is important to distinguish between the actual feelings and sensations of the patient, and the interpretations or explanations he gives of them. A layman's diagnosis, while often interesting, is not what is most helpful to the physician. When a patient is asked how he suffers, he replies most often with a "diagnosis," saying that he has "rheumatism," or "catarrh of the stomach," or "heart disease." While the physician will, for the moment, patiently listen to such a statement, he should at once ask the patient why he thinks he has the trouble he mentions, and will put down as the complaint of the patient, not the latter's diagnosis, but (1) any objective changes the sick person has noted himself and (2) the subjective symptoms upon which the layman's diagnosis is based.

(*a*) *The Present Illness*

After recording the name, age, occupation, and residence of the patient, the date on which he is first seen, and the chief complaints for which he seeks medical help, it is well to ask particular questions about the present illness, when and how it began, whether it developed suddenly or insidiously, how it progressed, and any treatment followed before consulting the physician. Inquiry is made as to loss of weight or strength, as to capacity for work, or, if the patient be in bed, as to the time when he had to go to bed.

It is well to ask the patient, also, what he believes caused his illness, knowing, when the question is asked, that the sick man may be wrong in his belief. In this part of the anamnesis, important data regarding (1) a preceding trauma, (2) physical or mental overexertion, (3) dietetic errors, (4) exposure to cold and wet or (5) exposure to infection, may be obtained. If the patient suffer from an infectious disease, the possibilities of contagion from other cases in the home, in the neighborhood, in the school, or elsewhere, should be gone into.

After the patient has described, voluntarily, his main symptoms, it is well to inquire systematically regarding various subjective symptoms referable to different parts of the body. Among these may be mentioned pain (location, character, duration, time of appearance, things which influence it, etc.), headache (position, accompaniments, frequency), dizziness, ringing in the ears or tinnitus, appetite, nausea or vomiting, state of digestion, constipation or diarrhea, presence or absence of hemorrhoids, cough, sputum, dyspnea, palpitation, retrosternal pain, swelling of the ankles, micturition, nocturia, the sexual functions, sleep, memory, concentration of attention, depression, power of decision, fears, feelings of unreality, etc.

In framing the questions, one keeps in mind the commoner subjective symptoms associated with the different bodily systems (respiratory system, circulatory system, digestive system, urogenital system, locomotor system, nervous system, metabolic system, endocrine glands). A symptom referred to a definite organ may depend upon a distant, or a general, rather than upon a local, cause; thus, the complaint of dyspnea need not indicate a primary disease of the lungs or of the respiratory passages, but may be due to intoxication of the nervous system from renal disease, to anemia, or to some other cause. Similarly, a fast pulse (tachycardia) may not indicate a primary disease of the heart, but may depend upon an intoxication of the sympathetic nervous system due to disease of the thyroid gland (as in Graves's disease). When the subjective symptoms point with considerable certainty to some one of the several systems of the body, the investigation may be supplemented by a whole list of questions directed especially toward the condition of the system under suspicion.

(*b*) *The Previous History of the Patient*

After gathering the important data regarding the present illness, the earlier history of the patient may conveniently be gone into, especially with regard to (1) diseases of childhood, (2) post-childhood diseases, (3) the general bodily functions and the sexual life, and (4) the patient's habits, education and experience.

Among the **diseases of childhood** concerning which we inquire are included measles, German measles, diphtheria, scarlet fever, small-pox, affections of the lymph glands, tonsillitis, adenoids, rickets and convulsions.

Of the **post-childhood diseases** we inquire especially regarding infections like typhoid, malaria, pneumonia, and pleurisy, and then briefly record any other serious disease passed through. In "nervous patients," we inquire especially regarding earlier periods of strain, of "nervous breakdown," or of "fainting spells." In men, the existence of a preceding gonorrheal, luetic, or other venereal infection should always be asked

about, and if such an infection has existed, full details regarding it, and the treatment followed, should be recorded.

The **general bodily functions and the sexual life** should be inquired into, the latter to a variable extent in different cases. Here the tact and common sense of the physician must guide him as to how much questioning is necessary and will be helpful. Any unnecessary investigation of sexual matters is to be deprecated, but the physician must not shrink from any inquiry which may be of importance for the patient's welfare. In women, we inquire regarding menstruation, pregnancies, puerperal states, interrupted pregnancies, children born dead, etc. In men, we inquire regarding sexual power (potentia), sexual desire (libido), and, if necessary, regarding sexual excesses or abnormalities. Inquiry regarding venereal disease has already been referred to.

In inquiring into the **habits, education, and experience** of a patient it is necessary to know something of his social state (luxury, poverty) and of his mode of life (muscular and mental activities). Any possible injuries associated with his occupation should be considered. The use of stimulants, and especially any abuse of these, should be investigated (tea and coffee, tobacco, alcohol).

(*c*) *The Family History*

We next study the evidence regarding the nature of the germ plasm of the patient as judged of by the results of inquiries concerning his ancestors and his children, for we can get information regarding heredity only through data regarding either the antecedents (direct or collateral) or the descendants of the patient. We ask whether the father and mother are living, or, if dead, the age and cause of death, and what diseases they suffered from during their lifetime. Similar inquiries are made regarding the sibs (sisters and brothers), and the children of the patient. In some instances, further inquiries regarding the family history (uncles, aunts, cousins, nephews and nieces, etc.) may be desirable. Should the disease from which the patient suffers be one in which heredity is believed to play a part (diabetes, gout, alcoholism, nervous and mental diseases, lues, tuberculosis, endocrinopathies, hemophilia, etc.), it may be well to construct a family tree, using squares to represent the males and circles to represent the females, indicating, by some special shading, the persons in whom the disease appeared.

2. The Present State of the Patient (Status praesens)

After taking the anamnesis, the physician makes a record of his own objective examination of the patient, of the state in which he finds him (*status praesens*). It is customary to describe (1) the general condition

of the patient (attitude and gait, if up and about; position assumed, if lying in bed; state of nutrition; strength; general appearance and habitus; facial expression; speech; condition of skin; visible mucous membranes, and superficial blood vessels); and (2) the results of examination of the various organs and organ-systems of the body. This latter portion of the record may be made in either one of two ways. Some prefer to classify the findings under headings corresponding to the individual systems (circulatory, respiratory, digestive, nervous, urogenital, etc.); others like to classify the findings according to the regions which are most conveniently examined in succession (head, neck, thorax, abdomen, extremities), and, afterwards, the results of various laboratory tests are appended. For systematic analysis and description in a text-book, the former method offers especial advantages; but in practical application at the bedside, the latter method is the easier to follow.

(a) *The General Condition of the Patient*

i. Gait and Attitude

If the patient be up and about, we can form some idea of the state of his muscles, his nervous system, and especially his organs of equilibrium, from the position he assumes and the way he walks. The experienced physician can also, from the first glance at the patient, gather data which help him to "size up" the individual—to "place him"—physically, psychically, and socially. Occupation, study, and social surroundings leave their stamp upon the individual. The greater the physician's knowledge of the world, and the wider his experience among all classes of human beings, the more acute will he be, other things being equal, in his discernment at the first encounter with the patient. Insight into human nature, tact, sympathy, and good judgment are the qualities in the physician, which at the first meeting help to gain access to the patient's personality and to inspire his confidence.

The different forms of abnormal gait and attitude are described in the section on examination of the nervous system.

ii. Position of the Patient in Bed

The patient usually assumes the position which is most comfortable for him. If an unusual position is maintained, the reason for it should be sought; it may be the only position possible for the patient.

To a certain extent the breathing of a patient determines his posture in bed; the more marked the shortness of breath, the less possible is the recumbent posture. A patient may be compelled to sit up in bed in order to breathe (orthopnea). The details of the various postures assumed by patients have been made the object of an especial study by Ebstein (q. v.).

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iii. Height, Weight and Build

It is well to record the patient's exact *height* in cubic centimeters, to estimate from this, by one of the formulae available (see chapter on Obesity), what his ideal weight would be, and to place beside this his *actual weight* as determined by the scales. A note should be made also as to the *bony framework* (strong; delicate), the *musculature* (well developed; feeble), and the amount of subcutaneous *fat*. In connection with the bony framework, the "span" or distance between the tips of the fingers of the two hands when the arms are stretched out horizontally from the shoulders, and also the *form of the thorax* (normal, paralytic, pyriform, emphysematous, rickety, pigeon-breast, funnel-chest, etc.) should be noted. The *general habitus* of the patient should be recorded (habitus asthenicus, habitus phthisicus, habitus apoplecticus, etc.). In abnormal cases, besides

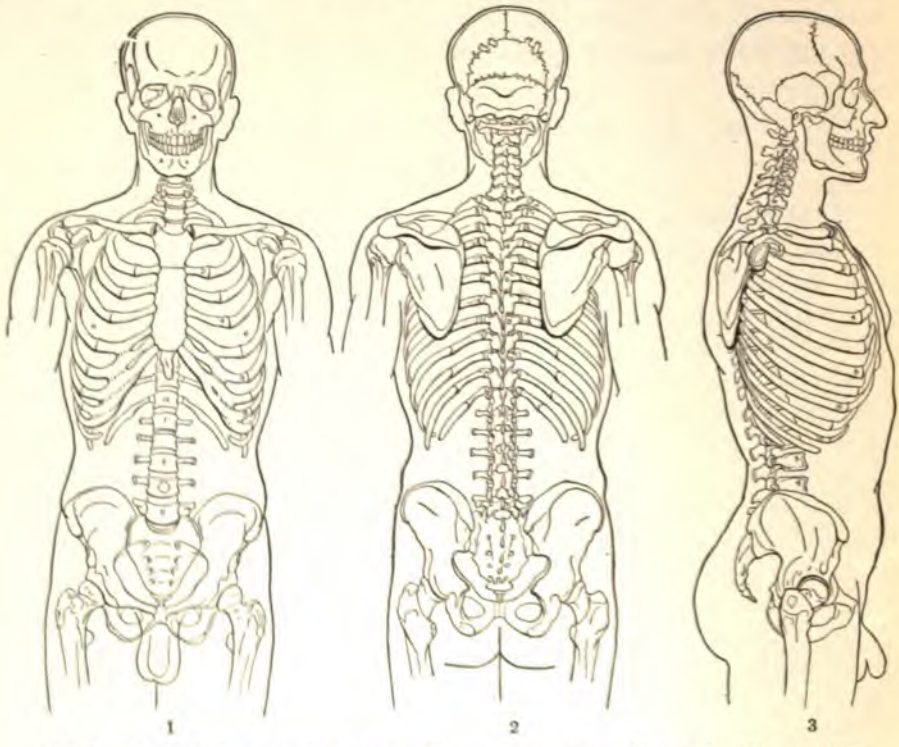
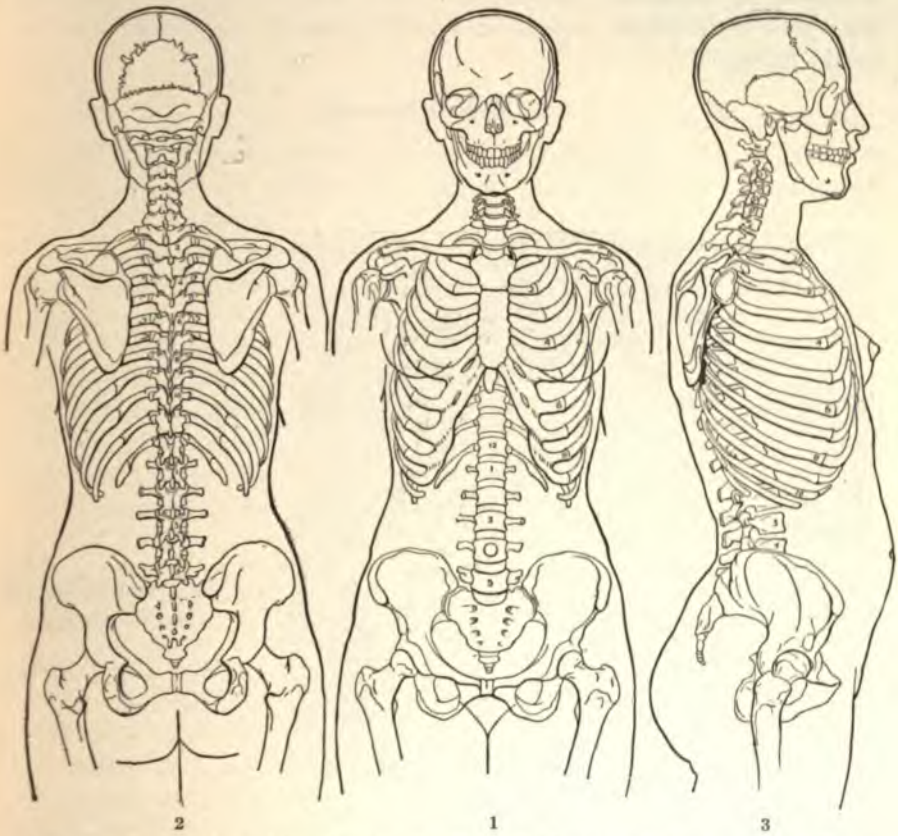


Fig. 1.—The Male Skeleton. 1—Anterior View; 2—Posterior View; 3—Lateral View.

the measurements of the epigastric angle, the so-called *Lenhoff index* may be determined—that is, the distance from the episternal notch to the symphysis pubis, multiplied by 100, divided by the minimal circumference of the abdomen. In normal women, in the recumbent position, this index



2 1 3

Fig. 2.—The Female Skeleton, 1—Anterior View; 2—Posterior View; 3—Lateral View.

averages 75. In men it is generally less than 75. A higher index (over 80) is met with in individuals with general visceroptosis (asthenia universalis congenita).

A note should be made of any anomalies of development (e. g., supernumerary fingers or toes; supernumerary nipples), or of any "stigmata of degeneration" visible.

iv. Mental State

At the very beginning of the objective examination, a note is made of the *general mental state* of the patient, whether he is conscious or unconscious, restless or delirious, and whether the state be one of apathy,

of stupor, of drowsiness (sopor) or of deep unconsciousness (coma). One notes whether the *speech* is normal or abnormal (hesitation, stuttering, syllable stumbling, dysarthria, asphasia, aphonia). One's first impressions regarding the *memory* of the patient for recent events, and his *mood* (depression, euphoria) should also be recorded. These first impressions may give clues for the course of a precise psychiatric examination to be made later.

v. Body Temperature

This is taken by means of a clinical thermometer, either by mouth, by axilla, or by rectum (see Diagnosis of Infectious Diseases), and the result recorded in a *temperature chart*, on which the number of respirations and the pulse rate per minute, the number of stools per day, and the amount of urine (in cubic centimeters) voided each 24 hours, may also be noted.

Fig. 3.—Supernumerary Nipples, when Present, Other Stigmata of Degeneration Should Be Looked For. (Medical Clinic, J. H. H.)

vi. Skin and Visible Mucous Membranes

The color, thickness and transparency of the skin are observed. An abnormal **pallor** may point to anemia, or at any rate to the necessity for a blood examination. After some experience one learns to distinguish between the pallor due to secondary anemias (following hemorrhages or wasting diseases) or to the pseudo-anemias (oligemia, etc.), and the peculiar waxy color of the skin seen in chlorosis (transparent yellowish white or alabaster white), or lemon-yellow tint or straw-yellow tint seen in the Addison-Biermer type of hemolytic anemia. Pallor is not always due to anemia, but may be due to a pseudo-anemia, in which there is an abnormally small supply of blood in the vessels of the skin (collapse, tobacco poisoning, mitral stenosis, syncope, aortic insufficiency).

An **abnormally red skin**, due to dilatation of the vessels, may be transient (blushing, emotional excitement), or more permanent, as in fever,

alcoholic intoxication, polycythemia rubra, or congestions of the head due to disturbances of sympathetic innervation.

Sometimes the skin looks bluish red, or cyanotic. When the whole skin assumes this color **(general cyanosis)** the cause may lie in general venous stasis, due to faulty action of the right ventricle (myocardial insufficiency; congenital heart disease), or to interference with the gas interchange in the lungs (dyspnea from various causes, emphysema, etc.), or, again, to polyglobulia.

A **local cyanosis** depends usually upon local obstruction (pressure, thrombosis) to venous outflow, or it may be secondary to hindrance to the arterial flow in the periphery, in which event the skin over the cyanotic part feels cold. In the latter case, the danger of gangrene should always be kept in mind. Among the forms of local cyanosis, or asphyxiation, may be mentioned: (1) that occurring in the fingers or toes in Raynaud's disease, and (2) that due to crises of arterial constriction in arteriosclerosis.

When the skin becomes **yellow,** due to the deposit in it of bile pigment, the sclerae of the eye beneath the conjunctivae will also be seen to be yellow. Such a discoloration, known as **jaundice,** or **icterus,** follows upon the entrance of bile into the general circulation (see Diseases of the Liver).

A peculiar **bronzed appearance** of the skin is met with in that remarkable disease of the suprarenal glands known as *Addison's disease.* The bronzing affects mostly the exposed parts of the body and those areas that are normally more or less pigmented (face, neck, waist, breasts, linea alba, axillae, perineum), as well as those that are exposed to the pressure of the clothing. The bronzing may affect the mucous membrane of the mouth, and, in white people, this is of diagnostic importance; "blue gums" in the negro may not represent any abnormality. The fingernails do not become pigmented in Addison's disease.

Another form of bronzing, usually not so dark as that seen in Addison's disease, is the brown discoloration met with in *hemochromatosis* (q. v.) and in the so-called "bronze diabetes," which so often accompanies its later stages. If a bit of the skin be excised for histological study, characteristic changes are found.

Local pigmentations in the skin follow upon local irritation of various sorts, especially in people of dark complexion; thus, after sunburn, exposure to the x-ray, the application of plasters or of heat, areas of pigmentation appear. Similarly, after skin lesions (eruptions, ulcers, herpes), the skin becomes pigmented. Pigmentation, associated with scratch-marks and filth of the skin, is common in pediculosis (*morbus vagabondi*). Sometimes, in pediculosis pubis, small blue spots (*tâches bleuatres; maculae caeruleae*) appear on the abdomen and on the thighs.

In pregnancy, the normal pigment deposits of the body are increased in amount (*chloasma uterinum*). In Graves's disease, in chronic tuber-

culosis, and in chronic lues, a general yellowish, or brownish, pigmentation of the skin is not uncommon.

Peculiar pigmentations of the skin may follow the use of drugs; thus, patients suffering from gastric ulcer or from tabes, for which silver nitrate has been taken over long periods, may exhibit a general, dirty gray, or bluish gray pigmentation of the skin known as *argyria*. If arsenic be taken for over three months at a time a general darkening of the skin not infrequently occurs (*arsenical melanosis*).

The skin varies in its **thickness** and in its **moisture**. A thick, dry, harsh skin is met with in myxedema; a thin, moist, transparent skin is common in Graves's disease. A fishlike, scaly skin is known as *ichthyosis*.

The moisture of the skin depends largely upon the secretion of sweat, which is under the control of the autonomic nervous system; thus, very abundant sweating (*hyperhydrosis*) is common in vagotonic states, while dryness of the skin (*hypohydrosis*) is common in sympathicotonic states. Sweats are common in the course of various infectious diseases (acute rheumatic fever, pulmonary tuberculosis, sepsis, malaria). After profuse sweating, it is common to find on the skin of the trunk numerous vesicles (*miliaria crystallina*), the size of a pin's head or smaller, which look like minute dewdrops. They are little retention cysts, due to temporary obstruction of the sweat glands. Sometimes the sweat is colored and stains the clothing; thus, in infections with the *Bacillus pyocyaneus*, the sweat may be greenish blue; in jaundice, it may be yellow. Red sweat, or so-called bloody sweat, has been shown to be due to the presence of the *Bacillus prodigiosus*.

Cutaneous eruptions (macular, papular, vesicular, etc.), or **exanthems**, should always be carefully studied; thus, *rose spots* upon the abdomen or back may be helpful in the diagnosis of typhoid fever. An early acquaintance with the eruption in the *acute exanthematous diseases* (scarlet fever, measles, chicken-pox, small-pox, etc.) is desirable, in order that humiliating mistakes may be avoided. The copper-tint common to luetic eruptions is very characteristic, and once observed, is easily recognizable.

If **hemorrhages** are present in the skin, their form, size and distribution should be noted. Minute, punctiform hemorrhages are spoken of as *petechiæ*; larger hemorrhages are referred to as *ecchymoses*, or *blood-extravasations*. Petechiæ should not be confused with minute *nævi* or *telangiectases*; when the latter are multiple they are sometimes associated with recurring epistaxis (Osler).

Petechiæ may be due to insect bites, to septic emboli of the cutaneous vessels, or to hemorrhages dependent upon diseases associated with the so-called *hemorrhagic diathesis*.

The presence of **ulcers**, **scars**, or **bed-sores**, and their size, location, and cause (when ascertainable), should be recorded.

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vii. Collateral Circulations

The existence of **dilated blood vessels** in any part of the body should be mentioned, if found; thus, *varicose veins* of the leg, *varicocele*, and *collateral circulations* should be looked for.

In **obstruction of the portal vein,** developing gradually (as in cirrhosis of the liver, or in lues hepatis), the blood from the portal domain finds its way into the venae cavae by three roundabout routes:

1. Through the anastomoses of the superior gastric veins with the esophageal veins to the vena azygos, accounting for esophageal varix and the hematemesis so common in cirrhosis hepatis;

2. Through the anastomoses of the inferior mesenteric veins with the hemorrhoidal veins (accounting for the anal hemorrhoids so common in cirrhosis hepatis and in chronic constipation);

3. Through the parumbilical veins (a) to the internal mammary veins and superior cava, above, and (b) to the inferior epigastric veins and the femoral and iliac veins and the inferior cava, below, thus accounting for those large tortuous "central veins" radiating out from the umbilicus and known as the *caput medusae* often seen in cirrhosis hepatis.

In **obstruction of the inferior vena cava,** from abnormal pressure of any sort in the abdomen, it is the lateral veins of the abdominal wall that are dilated in the formation of the collateral circulation, rather than the central veins mentioned above as concerned after portal obstruction. Here, also, the venous outflow from the lower extremities is interfered with (cyanosis; edema).

Fig. 4.—Obstruction of the Inferior Vena cava. (Med. Clinic, J. H. H., after J. Hall Pleasants.)

In cirrhosis hepatis, with ascites, there may be obstruction both of the portal circulation and of the circulation through the inferior vena cava.

Pulsating subcutaneous arteries on the trunk may be observed in instances of congenital narrowing of the aorta.

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viii. Edema

In *edema* of the skin and of the subcutaneous tissue, there is an increased amount of fluid in the tissues; the part is swollen, tense, and, sometimes, glistening and pale. In non-inflammatory edema, the part is not painful. When pressed upon with the finger, a depression remains for some time after the pressure has been removed. In edema of the extremities, the normal contours disappear. In fresh edema, the skin is easily indented with the finger-tip, but when the edema has lasted a long time this grows ever more difficult (boggy edema; tough edema).

When edema exists, its cause should always be sought. While in all cases edema arises through disturbance of the relation between the formation of lymph and the outflow of lymph from the tissues, this disturbance can arise from several different causes. It may be due:

1. To venous stasis (**stasis edema**), then occurring first in the depend-

ent parts of the body, the ankles on standing, the back and hips when in the recumbent posture;

2. To the injury of the blood vessels of the skin occurring in acute nephritis **(nephritic edema)**, then appearing, usually, first in the face, and especially in the loose subcutaneous tissue of the eyelids; [1]

3. To various inflammations and intoxications in which no evidence of cardiac or renal disease exists **(cachectic, toxic** and **inflammatory edemas)**, as, for instance, in the course of malignant neoplasms or the severe anemias, or in "serum disease";

4. To abnormal autonomic innervations **(angioneurotic edema,** or **Quincke's edema)**, as in transitory edema of the upper lip, the parts about one eye, etc.

ix. The Lymph Glands

In healthy individuals, the lymph glands are scarcely palpable, but in pathological states they may become enlarged, either all over the body, or (and this fact is very important for diagnosis) in the regions closest to some diseased part or organ. When enlarged, they can be felt as round or bean-shaped lumps, singly or in groups, in the subcutaneous tissue. One should ascertain whether or not they are soft or hard, tender or painless on pressure, discrete or matted together and adherent. It is well, in every case, to palpate systematically the principal accessible lymph-gland areas (epitrochlear, preauricular, submaxillary, retrocervical, jugular, supraclavicular, infraclavicular, axillary, paramamillary, thoracic, abdominal, inguinal, popliteal). If there is general enlargement of all the glands, one thinks of some general infectious or toxic process (syphilis, tuberculosis, Hodgkin's disease, infectious polyarthritis, leukemia, aleukemic lymphadenosis, etc.). If there is swelling of certain groups only, one looks for local infections in the regions drained by the particular group concerned (tuberculosis, pyogenic infections, plague, local arthritis, chancres, eczemas), or for some neoplasm metastasizing in the glands (carcinoma). (A fuller account of the diseases affecting the lymph glands will be found in Part VII.)

(*b*) *The Condition of Special Regions and Systems*

The further course of the objective examination of the patient will depend, for its order, upon which of the two plans already mentioned—(1) that of *regions* and (2) that of *organ-systems*—is adopted.

i. Examination According to Regions

Those who prefer, on account of convenience, to examine the body by regions, irrespective of the systems of organs in each region, will, after

[1] The edema occurring in contracted kidney is rarely a nephritic edema in the sense mentioned, but is most often a stasis edema due to myocardial insufficiency.

making notes on the general state of the body, examine systematically and record their findings in the following regions:

1. **Head** (skull, face, eyes, ears, nose, lips, mouth cavity, tongue, throat).
2. **Neck** (form, thyroid, lymph glands, skin, vessels, larynx, esophagus, cervical spine).
3. **Thorax** (inspection, palpation, percussion, auscultation, mensuration).
4. **Abdomen** (inspection, palpation, percussion, auscultation, mensuration).
5. **Extremities** (condition of skin, bones, joints and muscles; motility, sensibility, reflexes, etc.).
6. **Laboratory examinations** (urine, sputum, stomach juice, feces, blood, cerebrospinal fluid, x-ray examinations, etc.).

ii. Examination According to Systems

Those who follow the second plan, and make their examinations more strictly according to the individual organ-systems, independent of the body regions, will group their findings, say, under the following headings:

1. **Osseous system** (skull, spine, thorax, pelvis, extremities).
2. **Skin and subcutaneous tissue** (color, elasticity, turgor, moisture, edema, exanthems, pigmentations, striae, scars, collateral circulations).
3. **Muscular system** (atrophy, hypertrophy, electrical examination).
4. **Joints** (mobility, swelling, pain, x-rays).
5. **Lymph glands** (enlargements, consistence, etc.).
6. **Circulatory apparatus** (pulse and pulse-tracings, blood pressure, inspection, palpation, percussion and auscultation of heart, functional tests, röntgenoscopy, teleröntgenography, electrocardiography).
7. **Respiratory apparatus** (thorax anomalies; respiration; inspection; palpation, percussion and auscultation of lungs; sputum; nose; paranasal sinuses; larynx; transillumination; röntgenoscopy; röntgenography).
8. **Digestive apparatus** (mouth, tongue, pharynx, esophagus, stomach, intestine, liver, pancreas, spleen, functional tests of secretion and motility, röntgenoscopy and röntgenography).
9. **Urogenital apparatus and urine** (kidneys, bladder, genitals, urine).
10. **Blood and blood-building organs** (hemoglobin, enumeration of formed elements, fresh blood slide, dried and stained smears, parasites, bacteriological and serological examinations).
11. **Nervous system and sense-organs** (mental state, common sensibility, organs of special sense, motility, coördination, reflexes, autonomic functions, speech, identification, praxia).
12. **Metabolic functions and endocrine glands.**

13. Evidences of infection, immunity, and anaphylaxis.

Most clinicians come to some compromise between Plan I and Plan II. It is rarely that either plan is strictly followed.

iii. Combined Plan of History Taking

The following schedule is one found convenient by the author for his own clinical records.

I. Anamnesis

1. Preliminary Data: Name in full; age; state; occupation; home address; date of examination; chief complaint.

2. History of Present Illness.

A. Date and mode of onset; possible causes (intoxication, infection, physical or psychic trauma, occupation injury, dietetic errors, exposure to cold or wet, exposure to contagion); course from beginning to time of consultation; treatment followed hitherto.

B. Epitome of symptoms existing at time of consultation (pains; headache; dizziness; visual or auditory disturbances; cough; sputum; dyspnea; palpitation; appetite; nausea or vomiting; eructations; constipation or diarrhea; hemorrhoids; sweats; sleep; urine; nocturnal micturition; changes in body-weight; menstruation; libido; potentia; nervous or mental symptoms).

3. Previous History of Patient.

A. Diseases that the patient has earlier had.

(a) *Diseases of childhood:* measles, scarlet fever, diphtheria, "scrofula," congenital lues, etc.

(b) *Post-childhood diseases:* infections (typhoid, pneumonia, acute rheumatic fever, tonsillitis, gonorrhea, lues); diseases of various systems (circulatory, nervous, etc.); surgical operations.

B. Remarks on the general bodily functions (inclusive of the sexual) in earlier life; respiratory; circulatory; digestive; urogenital; nervous.

In women: menstruation; births; puerperal periods; miscarriages; chlorosis.

In men: libido; potentia; sexual excesses; pollutions.

C. Habits, Education, Experience:

(a) *Work;* exercise; rest; diversion.

(b) *Food* (amount; variety; time of meals; mastication).

(c) *Alcohol* (beer; wine; whiskey; cocktails, etc.).

(d) *Tobacco* (cigars; cigarettes; pipes; chewing tobacco; snuff).
(e) *Tea and coffee.*
(f) *Drugs* (trional; veronal, cocain; morphin; heroin; coca cola; bromoseltzer, etc.).
(g) *Education* (time; places; character).
(h) *Experience* (occupation; travel; social life, etc.).

4. Family History.

(A) Age if living, or at time of death, of (1) parents, (2) sibs (sisters and brothers), and (3) children. Health of each.
(B) Instances among near, or distant, relatives of diseases in which either *heredity*, or *contact*, may play a rôle (tuberculosis; syphilis; nervous and mental diseases; alcoholism; metabolic disturbances; endocrinopathies; neoplasms).

II. Status praesens

1. General Points.

A. Gait; attitude; posture.
B. Height; weight; build (habitus); nutrition; musculature.
C. Mental state.
D. Skin: Color (pallor, rubor, cyanosis), thickness, transparency, moisture, eruptions, edema, pigmentations, scars, striae, dilated veins, pulsating arteries.
E. Body-temperature. Striking phenomena ("snap-shot" diagnosis).
F. Lymph glands; bones; joints; muscles.
G. Radial pulse on both sides; blood pressure.

2. Regional Examination.

HEAD. Form of skull; facial expression; conjunctivae; eye movements; pupils; ears (tophi); hearing; sense of smell; nasal obstruction; lips; tongue; teeth; gums; throat; facial and lingual movements; speech.

NECK. Length and breadth; thyroid; larynx; trachea; tracheal tug; esophagus; blood vessels; lymph glands; cervical spine; cervical ribs.

THORAX. Form; epigastric angle; depressions or bulgings; dilated veins; breasts.

LUNGS.

Inspection. Respiratory movements: number; type (costal, abdominal, dyspneic, orthopneic, depth, symmetry); Litten's sign.

Palpation. Respiratory movements; vocal fremitus; friction fremitus.

Percussion. Lung limits; comparative percussion of two lungs.
Auscultation. Breath sounds; voice sounds; pleural sounds.

Heart and Aorta.

Inspection. Heart base; abnormal pulsations; apex beat.
Palpation. Apex beat; other pulsations; shocks; thrills.
Percussion. Superficial and deep cardiac dullness; retrosternal dullness.
Auscultation. Heart sounds; aneurysmal bruit; pericardial sounds.

Abdomen and Pelvis.

Inspection. Form (retraction, distension); position of umbilicus; changes during respiration; tumors or other bulgings; collateral circulations; visible peristalsis; hernias; strength of Mm. recti.
Palpation. Rigidity; local or general tenderness; hernial sites; tumor masses; stomach; intestine (small; appendix; cecum; transverse colon; sigmoid); spleen; liver; pancreas; kidneys; suprapubic region; inguinal regions; rectal examination; vaginal examination; genitals.
Percussion. Ascites; meteorism; stomach; liver; spleen; bladder; uterus; tumor masses.
Auscultation. Friction sounds; aneurysmal bruits.

Nervous System.

Sensory. Cutaneous and deep sensibility; stereognosis; sight; hearing; taste; smell.
Motor. Muscular power; finer movements; coördination; tonus.
Reflexes. Pupils; knee-jerks; ankle-jerks; periosteal radial; biceps and triceps jerks; plantar and abdominal reflexes; sphincters.
Autonomic. Vasomotors; secretory; trophic (sweat-glands, nails, hair, skin, etc.)
Psychic. Orientation; memory; calculation; attention; hallucinations; delusions; mood, etc.

Laboratory Tests (*Routine*). Urine; blood; sputum (if any); Wassermann.

Laboratory Tests (*If indicated*). Stomach juice; feces; cerebrospinal fluid; x-ray examinations; tuberculin tests; metabolic studies; electrocardiogram, etc.

3. Catamnesis

If the clinician is to profit by his experience, it is essential that he keep careful records of the history of his patients after they are first seen and examined, including the subsequent examinations made from time to

time, with observations upon the course followed by the disease, the kinds of therapy used, and their effects. Many hospital histories are fairly complete as far as anamnesis and status praesens are concerned, but are woefully lacking as regards the *catamnesis;* the same defect is too often true of the records kept by physicians in their private practice.

4. Epicrisis

Every practitioner of medicine should feel it his duty to contribute, whenever possible, to the advance of medical knowledge. He should be on the lookout for cases that can be of interest for science, and should see to it that such cases are thoroughly studied, and the results given to his fellow practitioners. Even if he be too busy to undertake the scientific studies himself, he should, when he recognizes suitable opportunity, call the attention of scientific workers to the case, and at least give them the opportunity of investigation.

In the *epicrisis,* the final judgment upon a case is recorded, with discussion of the meaning of the symptoms and signs. When an operation has been performed, or, in case of death, when an autopsy has been done, the findings are correlated as far as possible with the observations made before operation or before autopsy.

It would be well if every practitioner would go over his list of patients from time to time and attempt an epicrisis in each one. He will often be surprised at what he finds, and his clinical judgment should be greatly improved if he will follow the practice.

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C. General Remarks on Diagnostic Methods

The time-honored methods of physical examination—inspection, palpation, percussion, auscultation, mensuration—are still the most important diagnostic methods. To them have been added in recent years a large number of other methods—physical, chemical and biological—and many of these have now become indispensable for the diagnostician.

All methods of physical examination depend upon the utilization of the sense-organs of the examiner (sight, hearing, touch, temperature sense, taste, smell). The experienced clinician can make an extensive examination with his unaided sense-organs, but, as the science of medicine grows, the sense-organs of the examiner have to be aided by an increasing number of methods devised to extend these observing powers. Thus, through the help of the microscope (with or without the aid of selective dyes), the ophthalmoscope, the laryngoscope, the bronchoscope, the gastroscope, the sigmoidoscope, the cystoscope, the spectroscope, the colorimeter, the polarimeter, the refractometer, etc., the eye gains access to fields invisible without these accessories.

Through the stethoscope the ear can be made to hear sounds which would otherwise escape it; by means of the electrophonograph, sound vibrations at present inaccessible, even to the aided ear, can be registered and interpreted by the eye. Our impressions of the temperature of a patient gained through our own temperature sense are crude and inaccurate compared with the exact information yielded by the clinical thermometer. The palpation of the pulse by the fingers will tell much concerning the rhythm and the blood pressure, but instrumental methods of examination (sphygmograph, sphygmomanometer, electrocardiograph) permit of still more accurate analysis, and a comparison of the results obtained by the unaided sense-organs with those obtained by instrumental methods through a certain period of time greatly increases the knowledge obtainable by the former.

No hard and fast line can be drawn between clinical and laboratory methods. The use of our sense-organs (naked and aided) is common to both. Whether a given test shall be performed at the bedside, or in the laboratory, is merely a matter of convenience. There is no fundamental difference, in principle, in the two methods employed. One-sided views, however, are apt to prevail among men who work only at the bedside and who never make examinations in laboratories separated from the patient. The same is true of men whose circumstances confine them to laboratory studies and who do not come into contact with patients at the bedside. To prevent narrowness of view, it is desirable, either that one and the same man shall make both clinical and laboratory examinations, or that the men making bedside examinations predominantly shall be kept in

close and intimate relations with the men who are making laboratory tests predominantly. It is difficult for one whose work limits him largely to bedside examinations properly to value results of laboratory tests, unless he has had at least some first-hand experience with the laboratory tests themselves. Similarly, the judgment of the man whose work is predominantly in the laboratory will be better if he has had at least some training in the clinical methods of examination, and at least some experience in the course of disease as studied at the bedside. There is, undoubtedly, real difficulty at the present time, on account of the division of labor and the specialization of activity that the extension of the methods of clinical diagnosis has made necessary, in correlating all the results of examination that can be accumulated, and in arriving at a proper judgment regarding the condition of the patient as a whole. Upon a proper synthesis of the results, and upon the estimate formed of the relative importance of the various deviations from the normal, depends the therapy to be instituted. In this time of unprecedented specialism, there is greater need than ever for the all-around internist with sound judgment. The beginner, introduced to a great variety of specialistic methods, can scarcely avoid, at first, a feeling of bewilderment; do his best, he is likely to "lose sight of the wood on account of the trees." For this reason it is desirable that the young internist should work for a considerable period in close contact with, and under the direction of, clinicians of long experience; while perfecting himself in the technic of the single methods of examination, he will gradually learn, through the example of his more experienced seniors, how best to synthesize, and how adequately to value, the results of the physical, chemical, and biological investigations of the patients he studies.

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Part II

Examinations with Röntgen Rays (Röntgenoscopy; Röntgenography)

The Röntgen rays penetrate different parts of the body with varying degrees of facility; for the different tissues vary in their absorption of the rays, the air-filled lungs, for example, absorbing very few of the rays, the heart on the contrary absorbing them to a greater, the bones to a still greater, degree. It is accordingly possible, by means of photographic plates or of a fluorescent screen, to register, graphically, shadow pictures of the organs and tissues, corresponding to the differences in the penetrability of the parts by the rays.

A. Varieties of Apparatus for the Production of Röntgen Rays

Two fundamentally different kinds of Röntgen-ray apparatus are now available for röntgenological work:

1. An induction-coil apparatus with high-tension direct current and interrupter; and
2. A non-induction, interrupterless apparatus, with alternating current, step-up transformer, and high-tension rectifying switch that sends a unidirectional current into the x-ray tube.

Both of these apparatus can be used with either a direct or an alternating current; thus, for the inductor apparatus, an alternating current can first be converted into the direct current required; and for the non-induction, rectifying switch apparatus, a direct current can be converted, by means of an inverted rotary converter, into the alternating current required.

Coolidge has recently reported experiments that indicate that before long we may expect very definite improvements in the apparatus for producing Röntgen rays.

1. Röntgen Apparatus Utilizing Direct Current with Inductor

In this apparatus, an interrupter breaks up the high-tension dir current into single impulses, which arrive in the primary coil of t induction apparatus. On closure of the current, a magnetic field formed, which disappears again when the current is opened. In t secondary coil, an impulse is induced every time the primary current opened, and also when it is closed. For the x-ray tube, however, use made only of the induced current that arises on *opening* the circu A pulsating unidirectional current of sufficient intensity and tension obtained in the secondary circuit by an ingenious arrangement, throu

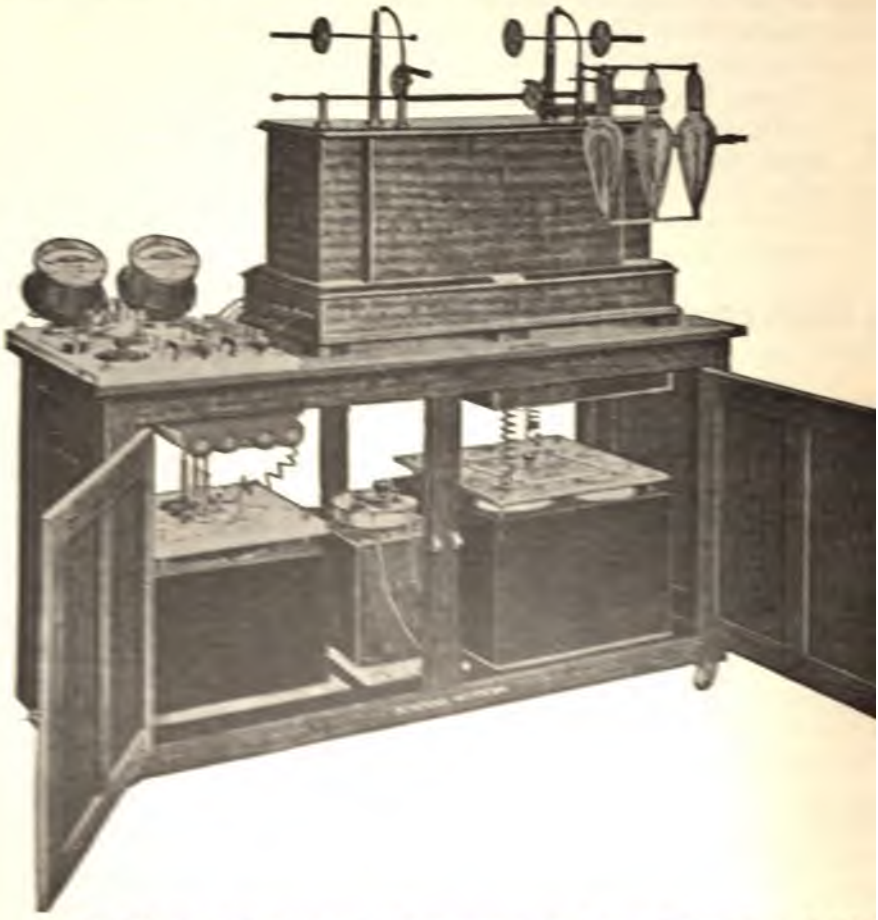

Fig. 5.—Induction Coil Apparatus. (By courtesy of the Schmidt-Western X-ray Coil Co.

which the opening current is made sudden and intense and the closing current as much as possible suppressed (condenser, jump-spark, or, better, "valve-tubes" that permit the current to pass through in one direction only).

(*a*) *The Interrupter*

The interrupter determines the rhythmical closure and opening of the primary circuit. Several varieties of interrupter are in use, the best ones being (1) a mercury centrifugal interrupter, in which contact with mercury closes, and contact with petroleum or alcohol opens, the circuit, and (2) a gas interrupter, in one variety of which, (a) the "apex interrupter," the current is made by contact with mercury, but broken by a gaseous dielectric (illuminating gas), and in another type, (b) Wehnelt's "electrolytic interrupter," gas is generated around a platinum electrode in quantity sufficient to interrupt the current.

(*b*) *The Rheostat*

A rheostat is intercalated in the primary circuit to regulate the intensity of the current by altering the resistance.

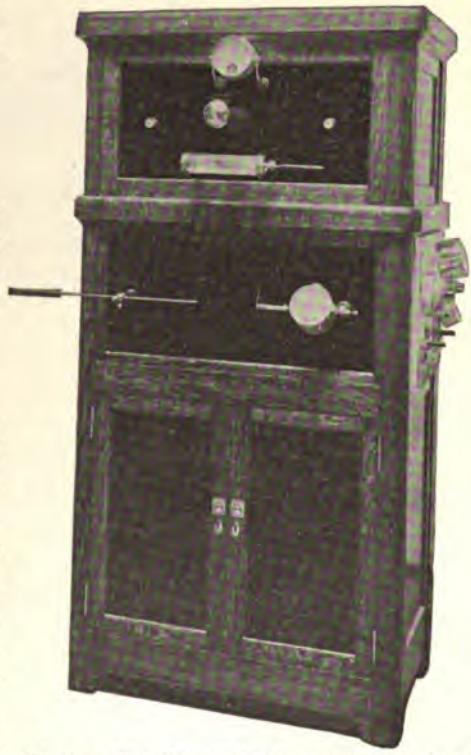

Fig. 6.—Apex High tension Generator. Model 1915. (By courtesy of the Kny-Scheerer Co.)

(*c*) *Single Impulse Apparatus*

The "single impulse Röntgen apparatus" is a modification of the inductor apparatus above described, especially adapted for "instantaneous röntgenography," the single "flash" lasting about 1/200 second. With this instrument, *moving organs*, like the heart, lungs, diaphragm, stomach, intestine, larynx on swallowing, etc., can be sharply outlined. It is useful, also, in making x-ray examinations in young *children*, in the *insane*, and in Parkinson's disease (*tremor*). The same machine can be adapted also for general work not requiring instantaneous exposures. This "single impulse" apparatus has contributed much to röntgen-cinematography.

2. Röntgen Apparatus Utilizing the Alternating Current with High-Tension Rectifying Switch

This apparatus does away with the inductor and the interrupter entirely, and is fast displacing the apparatus above described for general x-ray work. Though it makes use of an alternating current (Snook's A. C. Machine), a form of the apparatus is made that will supply the alternating current required from a direct current by means of an inverted rotary converter (as in Snook's D. C. Machine).

Fig. 7.—Interrupterless Apparatus. Alternating-current Machine. (By courtesy of the Snook-Röntgen Mfg. Co.).

(a) *The Step-Up Transformer*

A step-up transformer raises the voltage to very high tension. By means of a switch, the ratio of transformation may be changed through the "taps" provided in the primary winding of the transformer; as a result of this adjustment, the transformer secondary voltage varies from

70,000 to 120,000 volts. A rheostat in the primary circuit of the transformer regulates the current output.

(*b*) *The High-Tension Rectifying Switch*

The high-tension alternating current delivered by the transformer is carried through a high-tension rectifying switch, which changes it to a

Fig. 8.—Interrupterless Apparatus. Direct-current Machine.
(By courtesy of the Snook-Röntgen Mfg. Co.).

unidirectional current, suitable for use in x-ray tubes. In the A. C. machine, a synchronous motor drives the high-tension rectifier; in the D. C. machine, the rectifying switch is mechanically attached to the shaft of the inverted rotary converter and is thereby maintained in synchronism with the alternating current delivered by the converter.

When one has a choice, it is best to use an alternating current (220 volts, single phase, 60 cycles) as a source, and the A. C. machine. In buying a machine, it is necessary to know (1) what *kind* of current is available, (2) the *voltage*, and if the available supply be an alternating current, (3) the *frequency*, and the *number of phases*.

(c) *Advantages of the Rectifying-Switch Apparatus*

With this kind of Röntgen apparatus there are several distinct advantages, aside from its *noiselessness*, and its *simplicity*.

1. *Inverse discharge* is absolutely excluded.
2. Since there is no external magnetic field (a closed magnetic current circuit transformer being used, and the magnetic flux being confined to the iron of the

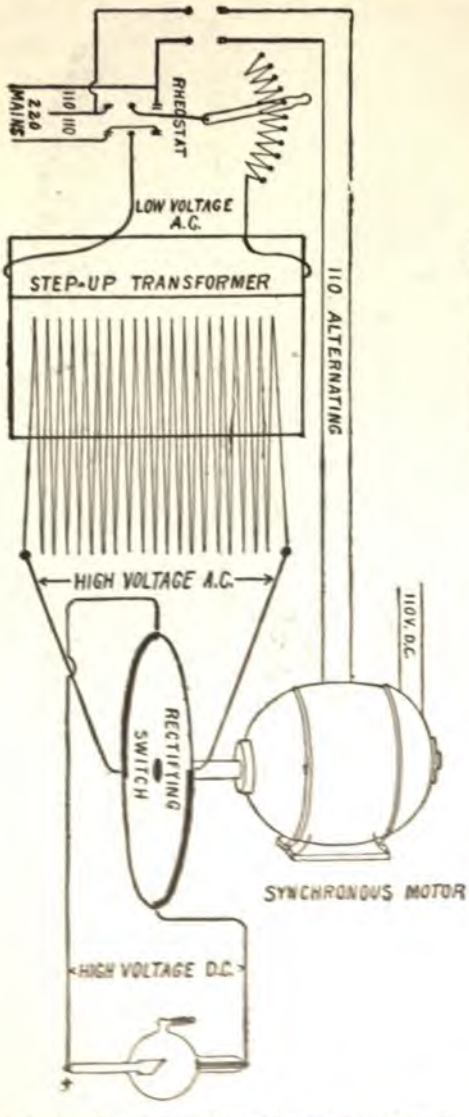

Fig. 9.—Wiring for Alternating-current Generator (Interrupterless Transformer Apparatus). (By courtesy of the Kelley-Koett Mfg. Co.)

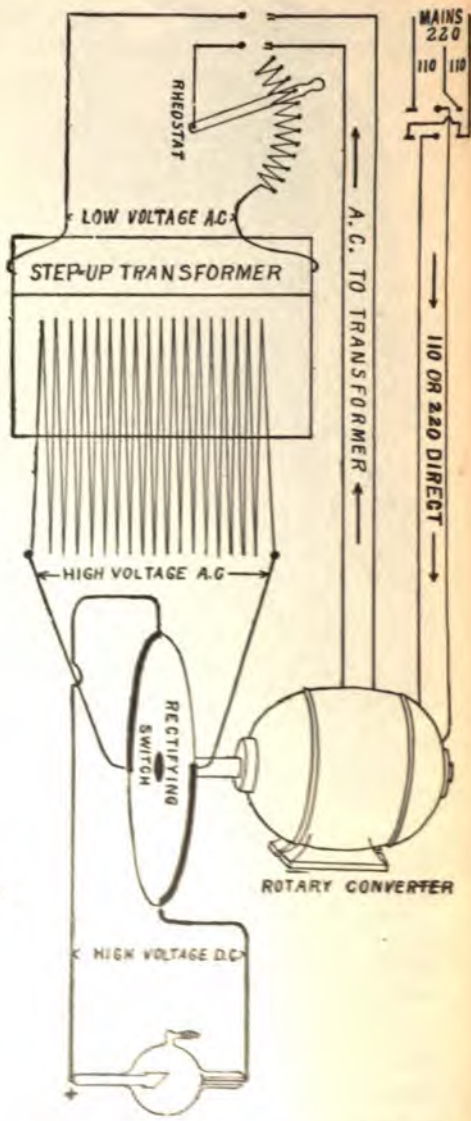

Fig. 10.—Wiring for Direct-current Generator (Interrupterless Transformer Apparatus). (By courtesy of the Kelley-Koett Mfg. Co.)

transformer), there is *no enlargement of the focus spot*, such as an external magnetic field may cause through its influence upon the cathode stream; when transformers with open magnetic circuits and induction coils are used, the focus spot of the tube wanders, and, dancing around on the target, results in blurring of the röntgenogram.

3. Very *short exposures* are possible, for the x-ray tube can be furnished with all the energy it can take unimpaired, and this energy-capacity of the machine is unassociated with any inverse-discharge; in the inductor apparatus, if the capacity is increased beyond a certain point, the "inverse discharge" becomes too strong for the x-ray tube, though with the "single-impulse" modification of the inductor-apparatus admirable instantaneous exposures are obtainable (see above).

4. The *x-ray tubes are protected* wonderfully and will last much longer than with the inductor apparatus; this is accounted for by the absence of "inverse," and by the lessened "digging" of the target.

5. The *current measurements are absolutely reliable*, and one can be quite sure just what x-ray effect is obtainable with a given tube and a given adjustment; with the inductor apparatus, there are so many variable factors that no equivalent certainty is possible.

6. The mixture of x-rays given out by tubes used with this machine is *very rich in "soft rays"*; an extraordinary richness of detail in the röntgenograms, especially of soft parts like the lung tissue, is attainable. Very much softer tubes can be used than with a coil apparatus.

7. By means of a "triple reel" attachment, the operator can *control and measure the tube-vacuum* from his position at the switch table; there is no danger of ruining tubes by "arcing" at the regulator.

8. An especially designed fluoroscopic attachment permits the operator to *use a tube for the maximum length of time with a minimum of heating and of drop in vacuum*. By simply moving a switch, a change to a heavy current for radiographic work can be made immediately.

9. For general *röntgenography and röntgenoscopy and for surface therapy*, this form of apparatus is by far the best; for deep therapy, especially for intensive therapy in the depth, the inductor apparatus is said to be better. When one has both inductor apparatus and rectifying-switch apparatus at one's disposal, the former may be used for depth therapy and for fluoroscopic work, the latter for all other x-ray work. Great advances in deep therapy have resulted from the introduction of the Coolidge tube.

B. The X-Ray Examining-Room

Now that röntgenoscopy or fluoroscopy (transillumination by x-rays; view on fluorescent screen) has become so helpful in medical diagnosis, and röntgenography (use of photographic plates) is indispensable, in both medicine and surgery, an x-ray examining-room should certainly be available in every town, and many individual practitioners are installing outfits of their own.

A *commodious room* that can be made absolutely dark is necessary, and the examiner should, for röntgenoscopy, adapt his eyes to the dark for five or ten minutes before making his examination.

In order that there may be a little light in the room between röntg-

genoscopic examinations, a *weak green light* placed close to the ceiling can be used and is the best. One can install a four-candle power, green-colored bulb, mounted in an "indirect" fixture; it should have a pendant, or a switch-control, operable from the position occupied by the examiner.

The room should be *well ventilated*, by light-tight methods through the doors and windows; electric fans are objectionable as they cause too much draught for an undressed patient.

The *walls* of the room should be painted a dull bluish gray, or a light gray containing a little red; they should *not* be black or dark red.

The *floor* should be of hard wood (parquet), *not* of linoleum, cement, or tiles.

Nearby, a convenient *photographic dark room* should be provided; it should be kept dry, clean, and orderly, and should have a supply of running water, a sink, a work-table with shelves, and red and white light, or Caldwell's ruby light. It should be properly warmed in winter.

In order to *protect the examiner and the patient* from harmful effects of the rays the x-ray tubes are nowadays provided with protective *lead-glass shields* (50 per cent. lead). In addition, a *lead screen*, 3½ ft. wide and 4½ ft. high, with a foot of transparent lead-glass above it, affords additional protection. Protective *gloves* and lead-glass *spectacles* are also available.

While most x-ray examinations are made of persons who can sit up or stand up, it is sometimes important to have an x-ray photograph or a fluoroscopic examination made of a patient so sick that he must keep the recumbent position. Movable x-ray *tables* have been constructed with the x-ray tube underneath; with such a table, the very sick pneumonia patient can, if deemed necessary, be photographed.

C. Röntgen Tubes

1. Structure of a Röntgen Tube

The x-ray tubes, used for the production of Röntgen rays, consist of spherical flasks in which a high-grade vacuum is produced by means of a mercury pump and heat; these flasks are provided with several attachments for special purposes.

Each tube contains three mirrors: (1) an **anode mirror**, connected with the positive pole of the high-tension current deliverer, this mirror being replaced in the newer instruments by a rod—the "anode rod"; (2) a **cathode mirror** (concave), connected with the negative pole of the current deliverer; and (3) an **anticathode mirror**, or **target**, consisting usually of platinum (iridium, tungsten, or tantalium), placed opposite the

cathode mirror at an angle of 45° to the axis of the tube. Outside the tube, the anode and the anticathode are united by a conductor.

2. The Röntgen Tube in Action

When the tube is in action, particles are driven off from the cathode (the so-called **cathode-rays,** visible in the form of a fine blue bundle) and strike upon the anticathode mirror or target, being roughly "focused"

A—Anode.
B--Assistant Anode.
C—Cathode.
D—Regulating Chamber.
F—Regulating Adjuster.
G—Hemisphere.
H—Connection Wire.
I—Assistant Anode Cap.
K—Anode Cap.
L—Cathode Cap.
M—Cathode Stream.
N—Focal Point.

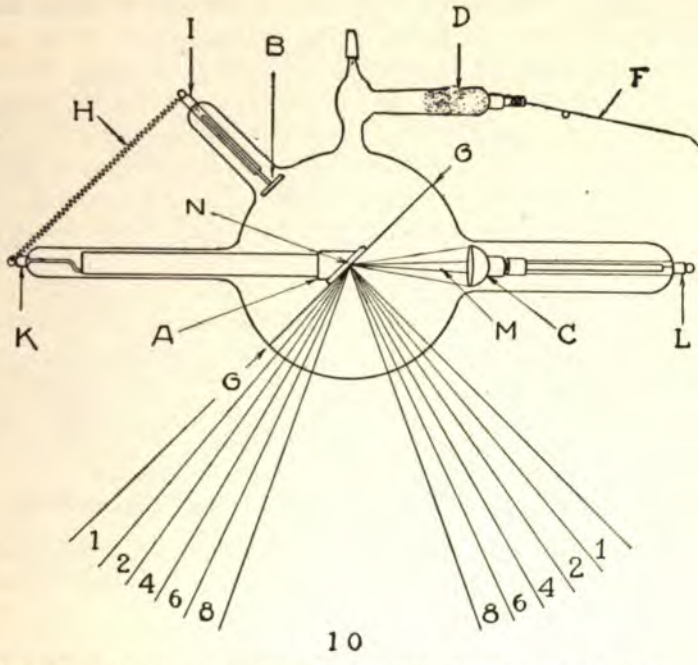

Fig. 11.—Diagram of a Röntgen Tube. (By courtesy of the Scheidel-Western X-ray Coil Co.)

upon it through the concavity of the cathode mirror.. They give rise, on striking the target, to the **Röntgen rays,** or **x-rays,** which pass off in all directions toward the half of the tube faced by the target (Fig. 11).

(*a*) *The Focus of the Cathode-Rays*

A "sharp" focus of the cathode stream favors the clearness of röntgenograms; but for röntgenoscopy and for therapeutic use of the rays, it is better to have the focus less sharp, since the anticathode plate tends to become very hot, and, on longer use, will burn through or be badly "dug out" if the cathode stream is too sharply focused.

(*b*) *The Normal Radiation*

The greatest Röntgen energy is possessed by what is known as the **normal radiation.** By this is meant the pyramid of x-rays emerging from the anticathode at approximately an angle of 90° to the bundle of cathode-rays.

(*c*) *Glass-Rays and How to Stop Them Out*

When an x-ray tube is working right, about one-half of the tube is brightly illuminated, while the other half remains darker, the junction between the two halves lying in the plane of the anticathode mirror. The illuminated half has a soft yellowish green fluorescent look due to the fact that not all the cathode-rays striking the target are transformed into x-rays; part of them are reflected and thus hit the glass wall of the x-ray tube, where they are converted into x-rays, at the same time causing fluorescence of the glass of the tube and warming of the glass. The x-rays thus produced are known as **glass-rays,** to distinguish them from the x-rays originating at the anticathode. These glass-rays, since they proceed from a widespread surface, are very diffuse in their distribution, and so are prone to cause blurring of the x-ray shadows. In order to avoid this blurring, as many of them as possible are cut off by means of a **diaphragm** interposed between the x-ray tube and the organ to be photographed, the diaphragm being placed as close to the x-ray tube as possible.

(*d*) *Coolers of the Anticathode*

Various forms of cooling apparatus are used to prevent melting of the metal of the anticathode (water-cooled tubes, metal-cooled tubes, air-cooled tubes).

(*e*) *Soft and Hard Röntgen Tubes*

As has been said, the Röntgen rays have different degrees of penetrability, according to the velocity of the cathodal x-rays producing them, this velocity in turn depending upon the grade of vacuum in the x-ray tube; the higher the grade of vacuum, the greater the average penetrability, or hardness, of the Röntgen radiation. The reason for this lies in the fact that a higher tension of the electric current fed to the tube is needed to overcome the internal resistance of the tube when a high-grade vacuum exists, and this high tension gives the cathode-rays a greater velocity.

Since the x-rays are always produced by single high-tension impulses, it is probable that the radiation is never homogeneous, but consists of a mixture of rays of the most different penetrating capacity, the composi-

tion of the mixture depending upon the discharge curve of each single impulse of the current sent into the tube. The form of the discharge in the rectifying-switch apparatus is such that the number of rays of variable hardness given off, especially of soft rays, is large. This is a real advantage, since the parts of the body of variable absorption capacity are much better differentiated on the fluorescent screen or in the photographic plate when the soft rays are abundant. With the older forms of inductor apparatus it was impossible to get good pictures of soft parts. The introduction of the rectifying-switch apparatus has led to enormous improvements in the detail of the negatives.

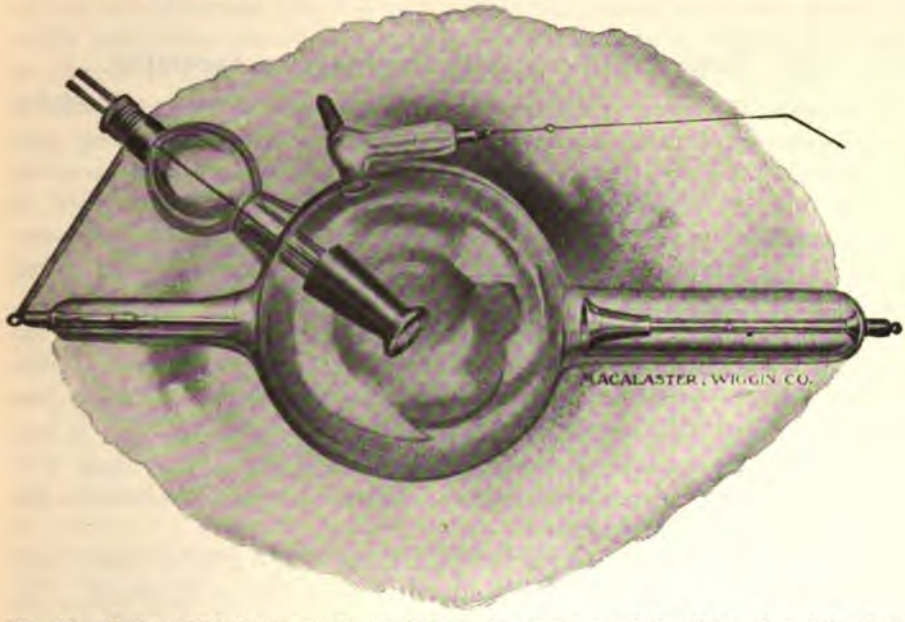

Fig. 12.—Water-cooled Tungsten Target Tube. (By courtesy of the Kelley-Koet Mfg. Co.)

It is, accordingly, customary to divide Röntgen radiations into (1) very soft, (2) soft, (3) medium, (4) hard, and (5) very hard radiations.

Anyone who works with x-ray tubes soon learns to distinguish the kind of radiation being sent off by a tube from its appearance in action.

In **very hard tubes,** streaks of light fly through the air outside the tube, between the attachment of the anticathode, the tension of the current required for such a tube being so high that the current passes more easily through the air than through the tube.

In the **hard tubes,** so-called "hardness-spots" of bright light appear in the tube, and the glass neck of the tube near the cathode mirror becomes strongly illuminated. Great care must be taken in using hard tubes, for there is always danger that the glass wall of the tube may be perforated, in which case air will enter and ruin the tube.

In a **medium-soft tube,** one half of the spherical flask is brightly illuminated; the other half is much darker, the plane dividing these two halves being that of the surface of the target. The illuminated half of the tube presents a soft yellowish green fluorescence, due to the fact that some of the cathode-rays, striking the target, instead of being transformed like the majority into Röntgen rays, are reflected from it, so as to strike the glass wall of the tubes where they are converted into Röntgen rays, the glass-rays described above.

In a **very soft tube,** the whole tube is illuminated except the dark cathodal space, and the blue bundle of cathode-rays is easily visible.

(*f*) *Inverse Discharge with the Inductor Apparatus*

In using the inductor apparatus, one of the most troublesome difficulties is that of *inverse discharge*, the current passing the wrong way through the tube. Such inverse discharge can often be prevented, on using a new tube, by placing a resistance coil, or a fuse, in a glass tube in the connection between the anode and the anticathode outside the x-ray tube. After a few weeks' use, the connection can be made directly to the anticathode if desired.

When inverse discharge occurs through a tube, dust may come off the metal of the anticathode; after the tube has been removed and this metallic dust has cooled, much of the gas in the tube will become united to the glass walls, and this will make the tube very much harder than it was before. Or, the vacuum of the tube may become "unstable," being very hard one minute and very soft the next, swinging to and fro between the two extremes like a pendulum.

In older tubes used with the inductor apparatus, a grayish black layer on the walls can be seen, due to metallic dust from inverse discharge. The violet discoloration of the glass wall of old tubes is entirely different in origin, depending, as has already been said, on the separation of colloidal manganese from the glass.

Fortunately, all inverse discharge is avoided by the use of the rectifying-switch form of Röntgen apparatus described, and a soft tube can be used for a very long time without growing hard.

It is important that tubes should be exposed to exactly the electrical tension that is best suited to them. If a tube grow softer, it is a sign that it has been given too heavy a burden; if it tend quickly to become hard, it is a sign that it has not been sufficiently burdened.

Since tubes gradually become harder with time owing to the diminution of their gas-content (absorption by metallic dust, accumulation on the glass walls), it is well to make use of them according to their degree of hardness; thus, the young, soft, tubes (low grade vacuum) should be used for photographing thinner parts of the body, like the hands and feet,

while the older, harder, tubes should be used for photographing thicker parts (heart, kidney, hip-joint, etc.).

3. Regeneration of Röntgen Tubes

As tubes grow older and become harder, it may be necessary to increase the gas-content a little. This may be brought about by any one of several methods of regenerating the tubes ((1) *osmo-regeneration* of Villard, in which a palladium tube is heated and a little hydrogen enters the tube through the metal;[1] (2) *carbon-regeneration*, in which gas is driven out of carbon into the tube; (3) *condenser-regeneration*, for especially hard tubes (Gundelach); (4) *air-regeneration*, in which a little air is allowed to enter the x-ray tube through a porous plate—especially useful for fluoroscopic tubes).

4. Care of Röntgen Tubes

Each particular brand of tube requires special care, and full instructions should be obtained from the maker regarding the treatment of the tube. Certain general rules, however, which I epitomize from the article by Janus and Schittenhelm, should be kept in mind:

1. No opportunity for grounding of the high-tension current should be permitted.
2. For each tube there is an optimal current, and care should be taken not to feed the tube with a stronger, or a feebler, current than this optimal strength.
3. New tubes, or so-called young tubes, should be very cautiously used at first, with avoidance of too strong a current and of the passage of the current through the tube for a long period. In a few weeks a tube can be "trained," or "educated," so that it will stand longer exposures and stronger currents. Sometimes a new tube may be hard; if so, it should not be treated as though it were a tube that has become hard through age, but should be subjected to a regenerative process until it is soft, and then slowly "educated" to its maximal performance.
4. If a tube does not respond in the way expected, no attempt should be made to force it to do so by increasing the burden thrown upon it. Sometimes, in winter, simply warming a tube for a few hours before use will make it more responsive.
5. X-ray tubes should be kept absolutely clean, protected from dust, and the exterior of the tube should never be touched with the fingers.
6. When selecting tubes it is well to buy a few of the best makes, and to learn thoroughly how to use the tube chosen. It is a mistake to experiment with a whole series of different varieties of tubes, since each make demands special treatment. If one has from four to six good tubes of different degrees of hardness, he should keep them, when well "trained," for the particular purposes for which they are most adapted. It is, as a rule, a mistake to use one and the same tube for different purposes. Much expense will be avoided if this precaution is observed.

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[1] Holzknecht's modification of this form of regeneration is preferred by the Vienna school.

7. One should form the habit of testing a tube every time before use; its hardness should be measured, and its behavior under a definite strength of current (milliampèremeter) and voltage determined. If, when the tube is in use, the intensity of the current, as shown by the milliampèremeter, increases, the tube is becoming softer; one should at once lessen the burden thrown on the tube, or it will soon become too soft. If, on the contrary, the intensity of the current decreases (milliampèremeter), the tube is becoming harder and a heavier burden should be thrown upon the tube, though this is less important than when the tube is becoming too soft. The worker has himself to blame when tubes become softer; the softening is due either to his throwing the wrong burden upon the tube, or to the youth of the tube.

8. In order to avoid using the tube any longer than is absolutely necessary, thorough preparation of the apparatus, and of the patient, should precede the turning on of the current. With a burden of 25 milliamperes or more for a single second, a young tube may be completely ruined.

D. Origin, Nature, and Properties of Röntgen Rays

In order to understand the origin of the x-rays and their nature it is necessary to begin with a description of the so-called cathode-rays.

1. Cathode-Rays

In a vacuum tube like an x-ray tube, the electrode through which the electric current, when passing through, leaves the tube containing the rarefied gas is known as the **cathode**. From the surface of this cathode, during the passage of the current, little particles known as **electrons**, charged with negative electricity, are driven with tremendous velocity.

These electrons are extremely minute, probably not larger than 1/200 part of a hydrogen atom. When this cathode stream of electrons passes through the rarefied gas of the tube, the gas in the tube becomes illuminated, only the immediate neighborhood of the cathode remaining dark, forming the so-called **dark cathodal space**, the region poorest in electrons. The greater the rarefaction of the gas in the tube, the larger the area of the dark cathodal space, and the greater the *velocity* of the electrons in the cathodal stream. In a high-grade vacuum, the velocity may reach almost that of light (300,000 km. per second).

The electrons are *emitted in a straight line*, perpendicular to the surface of the cathode which ejects them. In the x-ray tube, the mass of the electrons in this cathodal stream form a bundle of rays—the **cathode-rays**—possessing peculiar properties:

1. They make glass, upon which they impinge, give off light, the color of the light (sometimes green, sometimes blue) varying with the chemical constitution of the glass.

2. They go off *perpendicular* to the plane of the cathode, being uninfluenced by the shape or position of the anode. When a concave cathodal surface is used, the rays converge more or less toward a *focus,* though the focus is not a precise one, owing to *deflection* of some of the rays through magnetic or electric forces, especially in the inductor apparatus (q. v.). This deflection, however, can be largely avoided by the use of the rectifying-switch apparatus. The higher the grade of vacuum and the higher the tension of the current delivered to the tube, the less the deflection of the rays.

3. The cathode-rays *heat* the object they strike, enormously, so that arrangements for *cooling the target,* which they strike, are necessary.

4. Cathode-rays can *cause chemical changes;* a photographic plate inclosed within an x-ray tube is affected more or less as it is by light.

5. Bodies struck by cathode-rays become *charged* with negative electricity.

6. Cathode-rays do not penetrate the glass wall of an x-ray tube, but are *absorbed* by it, the glass becoming illuminated and heated during the absorption.

7. Most important of all, when the cathode-rays strike an object, besides the development of heat, another *transformation of energy* takes place, in that, from the place struck, *another kind of ray* is emitted: namely, the *Röntgen rays,* or *x-rays,* discovered by Röntgen of Wurzburg in 1895. These Röntgen rays are of several different sorts, their character depending upon the velocity of the cathode-rays producing them. Thus, cathode-rays of greater velocity, in tubes with high-grade vacuum, yield *hard Röntgen rays* capable of great penetration, while cathode-rays of slower velocity, produced in x-ray tubes containing more gas, yield *soft Röntgen rays,* of less penetrability.

2. Nature of the Röntgen Rays

The nature of these rays is still under discussion. According to the view dominant at present, they consist of *pulses in the ether,* not unlike light rays. They are believed to be *electromagnetic waves* of very small wave-length; in other words, ultraviolet light rays of wave-length still smaller than those of the ultraviolet rays hitherto known. It is supposed that the smallest observed light wave is at least a thousand times longer than the greatest wave-length of a soft Röntgen ray, the hard Röntgen rays consisting of still shorter waves.

3. Properties of Röntgen Rays

(*a*) *Penetrability of the Rays*

The x-rays are capable of penetrating chemical substances in inverse proportion to their atomic weight; the greater the atomic weight, the greater the absorption of the rays by the substance. In bodies of complex composition, like the organs of the human body, the rays are absorbed in very different degree by different parts. This accounts for the shadows visible upon the fluorescent screen, and for the variable effects upon the photographic plate in röntgenography.

The penetrability of the Röntgen rays varies, according as they are soft or hard; that is, according to the velocity of the cathode-rays producing them.

(*b*) *Propagation of the Rays*

The Röntgen rays are propagated in straight lines, but in all directions in space. As far as is known, they do not undergo refraction, nor can they be deflected from their course; in this they resemble light rays, and differ from cathode-rays. It is possible that some of the x-rays, namely, those with the longest waves, can be bent by means of the crystals of certain minerals. Investigations of this point are now being made.

Unlike cathode-rays, the Röntgen rays cannot be deflected either by magnetic or by electric forces.

(*c*) *Secondary Radiation*

Bodies struck by Röntgen rays give off secondary rays which have properties quite similar to the Röntgen rays giving rise to them. The greater the penetrability of the Röntgen rays, the greater also the penetrability of the secondary rays to which they give rise. It is asserted that chemical substances of high atomic weight give off a *soft* secondary radiation. Such a secondary radiation is usually given off by large bodies and is therefore diffuse.

The reason why it is not possible to get sharply circumscribed margins to organs in x-ray pictures is due to the *blurring effect* of the diffuse secondary radiation. When a certain thickness of the body has been passed through by the x-rays, the diffuse secondary radiation becomes so great as to exceed in its effects those of the x-rays themselves, and a sharp picture can no longer be obtained. And if x-rays of higher penetrability are used, the secondary radiation becomes all the stronger and the result is worse. It should, therefore, be borne in mind that on working with the x-rays on the human body, we are not dealing with a pure absorption of the x-rays, but with *absorption and a simultaneous transformation* of the rays.

(*d*) *Excitation of Fluorescence*

Röntgen rays, like cathode-rays, are capable of exciting definite chemical substances, like calcium tungstate, barium platinum-cyanur, zinc-blend, etc., to *fluorescence*. Utilization of this fact is made in röntgenoscopy, where the *fluorescent screen* is used; a further application is the *intensifying screen* in röntgenography.

The fluorescence varies in color, according to the chemical compound excited. The illumination of the screen will, in some instances, continue after the current has been cut off (so-called "phosphorescence" seen in certain intensifying screens).

(*e*) *Chemical Effects of Röntgen Rays*

Röntgen rays act upon photographic emulsion in the same way as the light of the ultraviolet spectrum (visible and invisible). The *bromid of silver is decomposed* in the photographic plate. Upon this property, *röntgenography* depends.

Advantage is taken of this fact also in the invention of a method of *measuring Röntgen energy* quantitatively, in the so-called *quantimeter* of Kienböck.

Still other chemical processes occur, under the influence of Röntgen rays, and have been utilized for measurements of Röntgen energy, as, for example, the *formation of calomel* from a mixture of corrosive sublimate and ammonium oxalate (Schwarz), or of *iodin* from a solution of iodoform (Freund), or the *change of color* from a green to a brownish yellow in barium platinum-cyanur (*radiometer* of Sabouraud-Noiré).

An interesting chemical effect of the x-rays is often seen, in older x-ray tubes, in the glass opposite the anticathode; a bluish violet discoloration appears, due to the *separation of collodial manganese* from the other constituents of the glass.

The Röntgen rays are capable of *ionizing gases* so that they can conduct electricity. This fact is taken advantage of in the making of measuring instruments, for example, in the *ionto-quantimeter* of Szillard.

(*f*) *Biological Effects of Röntgen Rays*

The Röntgen rays can destroy living cells. Certain cells are much more susceptible to their influence than others. Therapeutically, advantage has been taken of this fact (1) to destroy the cells of the lymphadenoid and the myeloid leukopoietic tissues in the leukemias, (2) to render individuals sterile for eugenic, or other, reasons by killing the germinative parts of the sex glands, and (3) to destroy the smooth muscle cells of large uterine myomata, a procedure which bids fair to lessen the work of the operative gynecologist.

Unfortunately, repeated and prolonged exposures to the x-rays may sometimes excite the tissues of the skin to carcinomatous proliferation. Many a röntgenologist of the earlier days has already paid, or is now paying, the price of our then ignorance of how to protect the operator from the rays.

E. Qualitative and Quantitative Measurements in Röntgenology

It is astonishing how many röntgenologists work in a haphazard way, never resorting to accurate methods of measurement, though they now have at their disposal a group of methods which permit them to work precisely. It is true that an experienced röntgenologist may make fewer errors without measurements, than a tyro will make with a complete set of measuring instruments; but, other things being equal, the worker who constantly controls his apparatus quantitatively, calling to his aid the different forms of measuring apparatus, will be far more successful and will progress more rapidly in scientific röntgenology than he who eschews these methods. It is probably true that most of the failures in x-ray work, most of the time and material sacrificed, and, too, most of the harm done to patients, has been due either to a complete neglect to measure the degree of hardness of the radiation and its amount or to attempts at measurement by unskilled persons.

1. Measurements of Hardness

Among the many "hardness measurers" now available, those of Walter, of Wehnelt, and of Christen are perhaps the best known. Other hardness measurers or penetrometers are those of Benoist, of Beez, and of Bauer.

Fig. 13.—The Benoist Penetrometer. (By courtesy of the Kny-Scheerer Co.)

(*a*) *Walter's Penetrometer*

This consists of a lead disk, 2 mm. thick and about 20 cm. in diameter, containing 8 round openings, each measuring 6 mm. in diameter; each of these openings contains a sheet of platinum, varying in thickness (0.005; 0.01; 0.02; 0.04; 0.08; 0.16; 0.32; 0.64 mm). In front of the disk is a fluorescent screen (lead-glass, coated with barium platinum-cyanur).

On testing an x-ray tube, the number of circles visible increases with the penetrating power of the rays being tested; thus, a tube which illumi-

nates six circles is said to have a hardness of 6 on the Walter scale; one illuminating four circles has a hardness of 4 Walter-units, etc.

(*b*) *Wehnelt's Cryptoradiometer*

This instrument is known as a *Precision Cryptoradiometer.* It contains an arrangement by which a wedge of aluminium can be shoved past an opening in a protective plate, and its illumination compared with that of an opening filled by a silver plate 0.11 mm. thick. The wedge is shoved along until the two areas present the same illumination. The hands and face of the observer are protected by a lead plate. By means of an attached "cryptoscope," the test can be made outside the dark room.

Fig. 14.—Wehnelt's Penetrometer.

A simpler form of the Wehnelt apparatus has been devised, the reading of which depends upon an optical illusion. It is fastened behind the fluorescent screen. Behind the silver plate the screen fluoresces of course evenly, but the eye seems to perceive an unequal illumination. A pair of clear areas and a pair of dark areas lie diagonal to one another. The point at which these four areas meet gives the hardness of the radiation, which can be read off on a perforated copper scale on the fluorescent screen. This instrument is very convenient, since fairly accurate readings can be made with it at a glance. With the aid of the cryptoscope, this simple form also can be used outside the dark room.

(*c*) *Christen's Absolute Hardness Measurer, or So-Called "Half-Value Layer"*

By using this instrument, the attempt is made to do away with arbitrary values and to establish an absolute unit of measurement, the so-called "half-value layer"; that is, the thickness of a layer of water which will absorb half of the radiation striking it, the other half passing through.

As a matter of fact, water itself is not used, but, instead of it, a solid substance (bakelit), which has the same absorption capacity as water. The general make-up of the instrument resembles Wehnelt's cryptoradiometer, but instead of Wehnelt's aluminium wedge, we have, in Christen's instrument, an *échelon*, or staircaselike, graduation of the wedge, the individual

steps of the staircase being composed of the substance having the same absorptive power as water.

The illumination of a portion of the wedge is compared with that of an evenly perforated metal sieve. The latter yields a fluorescence illumination corresponding to "half-value" since the areas of the transverse section of all the sieve openings is equal to half the area of the transverse section of the whole sieve surface. By removing the sieve some distance from the fluorescent screen, the single fine openings in the sieve are not projected, but, instead, there is a homogeneous illumination of medium grade.

This absolute "half-value layer" represents a real advance in hardness measurement. With it, we can get a better idea of the penetrability of the x-rays than is possible by any other method; thus, for example, if the half-value layer, as measured, amounts to 0.6 cm., we know immediately

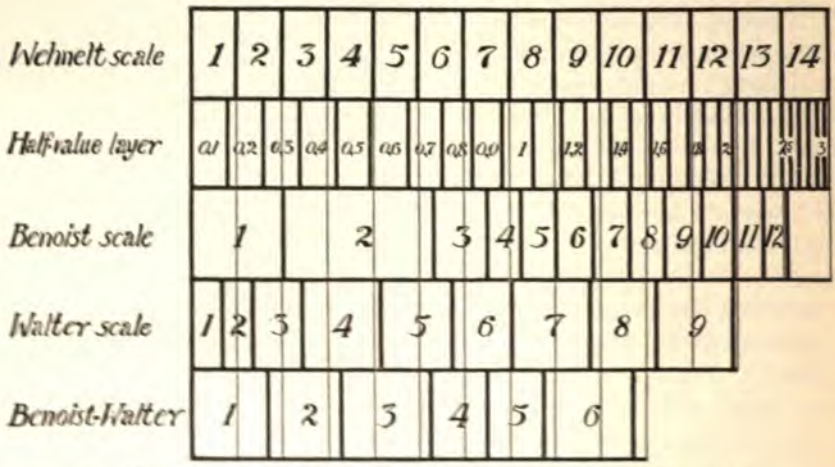


Fig. 15.—Comparative Scale for Penetrometers or Hardness Measurers.

that, at a depth of 0.6 cm., half of the radiation concerned is still active, and that at double this depth, i. e., at 1.2 cm., a quarter of the radiation is still active; at triple the depth (1.8 cm.) only a ninth, and so on. As Janus and Schittenhelm point out, this kind of measurement is especially valuable in therapeutic applications of the x-rays to the deeper tissues, for, if one knows the half-value layer and the dose of radiation, he is accurately informed as to the amount of radiation reaching to definite depths.

A special modification of the half-value measurer for photographic registration has been devised. In it, the *échelon* wedge is made in the form of a circle. The apparatus is laid on a photographic plate; a fly-wheel, run by clock-work, rotates, exposing the different parts of the wedge. The plate is then developed and fixed, and the hardness read off. This apparatus is especially helpful in scientific researches on the Röntgen rays.

2. Measurements of the Intensity of the High-Tension Current

In order to know the intensity of the current entering an x-ray tube, and, from it, to estimate the burden we are throwing upon the tube, a milliampèremeter can be intercalated in the high-tension circuit. It is desirable to use a large milliampèremeter, the scale of which can be seen, at a distance of 10 or 15 feet, in a darkened room. Since, for different purposes, different amounts of burden are thrown upon the tube, it is necessary that the milliampèremeter be provided with a wide range of measurement possibilities; thus, it may sometimes be desired to measure currents of low intensity say 0–5 milliampères, as in röntgenoscopy and in therapeutic applications of the x-rays, whereas, for röntgenography, stronger currents are used, for some tubes, 0–25 milliampères, for other tubes, especially for instantaneous röntgenography, 0–50 milliampères.

The intensity of the radiation sent out from the tube is approximately proportional to the intensity of the current flowing through the tube; in other words, if the intensity of the current be 10 milliampères, the x-ray effect will be about double that with a 5 milliampère current during the same time. It must be borne in mind, of course, that with currents of stronger intensity, the hardness of the tubes increases to a certain extent; in other words, a current of double strength will yield a little more than a double x-ray effect.

The milliampèremeter should be protected by a small condenser, placed parallel to it in the circuit; otherwise oscillating discharges may give rise to false readings. When the inductor apparatus is used, one may be deceived by readings affected by inverse discharge. This is avoided entirely in the modern form of x-ray apparatus, in which alternating current and rectifying switch are used.

3. Measurements of the Quantity of Röntgen Radiation

(*Dosage of X-Ray; Radiometry; Quantimetry*)

In therapeutic applications of the x-rays, it is essential to know the quantity of radiation that is being applied; otherwise x-ray burns of the skin, or wholly unexpected and sometimes dangerous x-ray effects on the organs, will be obtained. A number of *radiometers,* or *quantimeters,* have been introduced. Among these, the best types are: (1) Holzknecht's modification of Sabouraud and Noiré's radiometer, (2) Szillard's ionto-quantimeter, and (3) Kienböck's quantimeter.

(*a*) *Holzknecht's Modification of the Sabouraud-Noiré Radiometer*

In the original French instrument, circular disks 7 mm. in diameter, made of potassium platinum-cyanur, of yellowish green color, were

exposed at half of the focus-skin distance to the radiation; under radiation, the color changes gradually to reddish brown. This discoloration is compared in diffuse daylight with the discoloration which corresponds to an "erythema dose," that is, to that dose of Röntgen radiation that causes slight inflammation of the skin and falling out of the hair.

Certain precautions must be observed:

1. The exposure should be made in dim daylight only, owing to the fact that the pastilles are discolored by bright light; after the exposure, the comparison with standard color should be quickly made.

2. The stock of pastilles should be kept in a cool place, since heat discolors them.

3. Discoloration from the heat of the x-ray tube is avoided by placing the disks at least 2 cm. distant from the glass wall of the x-ray tube.

4. In making the test, the pastilles must be exposed to the same pyramid of rays as is used in the therapeutic treatment.

Fig. 16.—Sabouraud and Noirés Radiometer. (By courtesy of the Scheidel-Western X-ray Coil Co.)

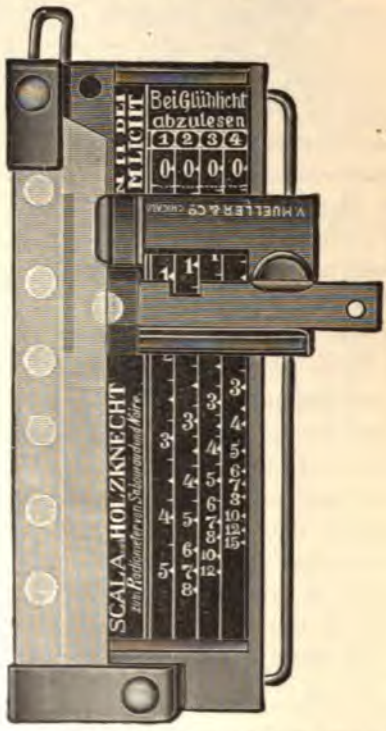


Fig. 17.—Holzknecht's Radiometer for Direct Reading of X-ray Dosage. (By courtesy of V. Mueller & Co.)

With the original instrument, only the maximal dose could be measured; with Holzknecht's modification, this objection is overcome, in that the discoloration of the exposed pastille is compared with the color of a fresh pastille which is shoved along beneath a strip of celluloid of increasing redness until the two colors are alike; on an adjoining scale, the "dose" can be read off.

(*b*) *Ionto-Quantimeter of Szillard*

This is an application of the fact that x-rays ionize air. The instrument consists of an ionization chamber, which is laid upon the area of

the body that is to be exposed. The instrument is wound up by turning a crank on one side until the indicator stands at zero. There is an adjustment by which the opening of the ionization chamber can be enlarged or diminished to compensate for variable grades of "hardness" of the radiation. Radiation is then begun and the advance of the indicator on the scale is observed. As soon as the dosage desired has been reached, the current is turned off.

(*c*) *Quantitimeter of Kienböck*

A small strip of photographic gas-light paper is inclosed in black paper, placed upon the surface of the body to be treated, and the exposure begun, the x-ray tube receiving a current of definite intensity (milliamperes), and the hardness of the tube having previously been measured. After a certain definite time-exposure, the gas-light paper is developed and fixed, and the blackening compared with that of a standard scale that permits one to read off the dose directly. The difference between this amount and the dosage decided upon is now known, and, as a control, a second strip of gas-light paper is exposed, while the remainder of the dose is given. This second strip is subsequently developed and fixed; its amount added to the amount indicated by the first strip, should correspond to the exact dosage determined upon beforehand.

Fig. 18.—Kienboeck's Quantitimeter.
(By courtesy of the Scheidel-Western X-ray Coil Co.)

I would call attention to the value of this method as a protection of the röntgenologist in medicolegal cases. If the strips of paper as developed are kept on file, they may form valuable evidence if the röntgenologist should be wrongly accused and subjected to lawsuit.

SCALE OF QUANTITY.

Holzknecht Chromo-Radiometer.....	1	1.5	3	4	**5**	6	7-8	14	20-22	Units H
Sabouraud-Noiré Radiometer.....					**B**					Tint
Bordier Chromo-Radiometer.....			0	0-I	**I**	I-II	II	III	IV	Tint
Kienboeck Quantitimeter.....	2	3	6	8	**10**	12	14-16	28	40-44	Units M
Schwartz Precipitation Radiometer		1	2		**3.5**					Kaloms

Fig. 19.—Comparative Scales of Quantitimeters.
(By courtesy of the Scheidel-Western X-ray Coil Co.).

F. Central Projection and Parallel Projection

1. Divergent Rays and Central Projection

When the Röntgen rays start out from the tube, the stream is only a few millimeters in diameter at the target, but the rays diverge, and an organ of the body placed between the tube and a fluorescent screen (or photographic plate) will appear in the picture in **central projection,** enlarged, owing to the divergence of the rays. The closer the plate or screen to the organ, the less the enlargement; this is why, on looking at the heart, the fluorescent screen is held over the heart in front, rather than behind.

2. Parallel Rays and Ortho-Projection

(*Orthodiagraphy*)

In order to determine the exact size of an organ by means of the x-rays, an apparatus known as the **orthodiagraph** was devised by Moritz, and later improved by Groedel. It has been especially useful in studies of the heart.

By this method, a complete **parallel projection** is made possible; it permits of an exact reproduction of the outlines of the heart, in natural size. This parallel projection is achieved by means of an apparatus which makes the x-ray tube movable, so that a very small bundle of the rays, from the

anticathode, can be made to move in all directions in a plane; the bundle of rays in the different situations follows lines which are parallel to one another. Thus the bundle can be made to move around the margin of the organ under observation (parallel projection); the x-ray tube and the marker, for recording the outline on the fluorescent screen, move as a single piece, being firmly united with one another. At many points, along the outline of an organ (first the right margin of the heart, then the left margin, then the diaphragm, the lung margins, and the lower edges of the

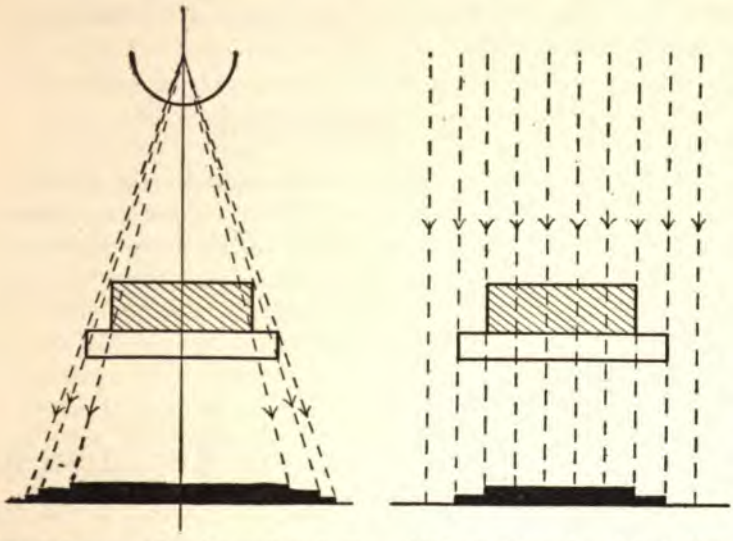


Fig. 20.—Ordinary and Orthogonal Projection. (After T. Brugsch and A. Schittenhelm.)

clavicles), a mark is made on paper by pressing on a rubber ball, and these marks are later united by lines to form the "orthodiagram." With more recent apparatus (e. g., Snook's vertical fluoroscope), the orthodiagraphic image is traced on tracing-glass with a grease pencil, the simultaneous movement of the tube and the tracing-pointer being accomplished by a set of large heavy metal parallelograms.

The **orthodiagrams** obtained over the normal heart and over pathological hearts are described in the section dealing with the diagnosis of circulatory diseases.

3. Teleröntgenography and Teleröntgenoscopy

Recently, it has been found possible to replace orthodiagraphy by the so-called teleröntgenography. By röntgenographing the patient at a distance of 2 meters from the x-ray tube, with a very short exposure (1/10–

1/8 second), a röntgenogram is obtained in which the heart is of almost natural size (Kohler), the error not exceeding 2 mm. for either margin of the heart. At this distance from the tube, practically a parallel projection is obtained, and the error no greater than with orthodiagraphy. If desired, the same principle can be used for fluoroscopic examination of the heart (making a drawing on the lead-glass of the fluorescent screen); for this purpose a drawing-stand, permitting of movement in two directions, is a great convenience.

Teleröntgenograms taken with the single impulse apparatus are said to yield very sharp pictures of the outlines of the heart as all blurring from pulsation is absent.

4. Diaphragms

In order to prevent blurring of the shadows by the glass-rays (q. v.) and by the secondary radiation (q. v.), it is necessary to use *diaphragms,* or, better still, *tubes,* through the openings of which the more central pyramid of rays is made to pass; in this way, sharper pictures, richer in contrast, are obtained. This helps especially in getting details of a lung apex, or of a kidney.

G. Photographic Technic in Röntgenography

A few practical points in the photographic technic may be mentioned.

It is best to use dry plates (bromid of silver), especially prepared for x-ray work (thicker film of emulsion). Plates of several sizes are required (8 x 10; 10 x 12; 11 x 14; 14 x 17).

It is false economy to use the cheaper varieties of plates.

Just before use, a plate may be placed in a *black envelope,* to protect it from the perspiration of the patient.

Each plate should be *numbered* by means of a röntgenographic "plate marker"; when helpful, the *right side,* or *left side,* should be marked (kidney). The plates should not be too old.

For röntgenography of the teeth, celluloid *dental films,* 1¼″ x 1⅝″, can be purchased; they come in small envelopes of black paper, ready for use in the mouth.

For developing the negatives in the dark room, a *slow developer,* capable of developing through the whole layer of emulsion to the glass, without fogging, is recommended; either a glycin-developer, or a metol-hydrochinon developer will be found satisfactory.

After development, the plates are fixed, being left in the *fixing-bath* twice as long as is necessary wholly to dissolve the bromid of silver; the *time* amounts to at least six or eight minutes. The plates are then washed thoroughly, in running water, for at least an hour, or in non-running water, changed four or five times, for at least two hours. Unless the fixing and washing is thorough, yellow spots will later appear on the negatives.

H. Clinical Applications of the Röntgen Rays

The shadow pictures obtainable, due to differences in absorption power of the different tissues of the body, are of the greatest help in clinical diagnosis. With Dr. F. H. Baetjer, the röntgenologist at the clinic in which I work, and with his associate, Dr. Waters, I have had manifold opportunity to observe the röntgenological shadow-pictures in all kinds of clinical conditions, and have come to rely upon röntgenoscopy and röntgenography as two of the most important aids in present-day clinical diagnosis.

In the *thorax,* the cardivascular stripe can be studied as well as the lung areas, the esophagus, and the mediastinal structures; tumors, pleural effusions, etc., can also easily be made out.

In the *abdomen,* by the introduction of contrast substances like barium sulphate into the gastro-intestinal tract, or thorium into the urinary tract, the form, position, and motility, of these organs can be accurately studied. Fistulæ can be filled with bismuth paste before study. Sometimes it is helpful to blow air into the intestine or into the bladder, before taking an x-ray photograph. The orthopedists have found help from oxygen injections into the *joint cavities,* before making the x-ray picture, in the differentiation of some forms of arthritis.

For some purposes, observation on the fluorescent screen **(röntgenoscopy)** is of greater value. In other cases, x-ray photographs **(röntgenography)** are more helpful. Thus, in the examination of the thoracic organs, and of the gastro-intestinal tract, röntgenoscopy is for most purposes best, though, for finer changes in the lungs, and for permanent records of momentary conditions in the abdomen, röntgenography is essential. In bone work and in genito-urinary work, röntgenography is more valuable than röntgenoscopy.

1. Technic of Röntgenoscopy

In röntgenoscopy the x-rays from the tube pass through the body and excite the fluorescent screen, held on the other side, into fluorescence. The parts that most completely absorb the rays appear, therefore, as shadows upon this screen.

(*a*) *Fluorescent Screens*

These consist of frames, containing a plate coated with a fluorescent substance, usually barium platinum-cyanur in fine crystals, imbedded in cellulose. The smaller the crystals, the sharper (though darker) the pic-

tures obtainable. By thickening the layer of the fluorescent substance, greater brilliance is obtainable, though the price is increased. Since the brilliance of the fluorescence depends upon the water of crystallization in the crystals, care must be taken not to drive off any of this crystallization water (by heat, pressure, scratching, etc.).

Fig. 21.—Lead-protected Röntgenoscope. (By courtesy of the Scheidel-Western X-ray Coil Co.)

A less expensive screen is the so-called "astral screen" (Rupprecht). It gives results fully equal to the platinum screen, and is not so easily spoiled.

To protect the examiner, the screen is covered with lead-glass, and if the screen is held in the hands, these should be protected by lead flanges, or the examiner may wear protective gloves. In the newer vertical fluoroscopes, the frame on the operator's side carries a 17″ x 17″ screen, covered with a special lead-glass, which stops all the direct rays that fall upon the screen. The operator is protected further from secondary radiation, by curtains of special material hung around the patient. Automatic protection is also afforded by mechanical devices that prevent too great a relative motion between the tube and the screen.

Larger screens are also now in use—18″ x 24″, 24″ x 30″, 30″ x 40″, 40″ x 50″. For most purposes, the smaller screen is sufficient. To make permanent records of the röntgenoscopic view, one can draw visible contours on the lead-glass surface with a grease pencil. After the examination is over, this outline is copied by means of tracing paper. The lead-glass plate is then rubbed dry and is ready for another examination.

Fig. 22.—Astral Screen for Fluoroscopy. (By courtesy of the Kny-Scheerer Co.)

(*b*) *Vertical and Horizontal Röntgenoscopy*

In most cases, the *vertical fluoroscope* is used, the patient standing, and the examiner sitting in front of him on an adjustable stool. Feeble patients may, when necessary, be steadied by a canvas band and two vertical rods by which they are held close to the screen. Children, even sucklings, can be fluoroscoped in the upright position by fastening them in a "baby's stand" (Grosser).

In the *horizontal fluoroscope,* the tube-case is placed under the examining table. Many varieties are available (Trochoscope; Universal Examining Table, etc.).

In simple röntgenoscopic outfits, tube stands, with lead-shields, are used, but, in the more expensive outfits, the tubes are held in tube holders inside a tube-box.

(*c*) *On Certain Details of Röntgenoscopy*

On account of the *long exposure* in fluoroscopy, special water-cooled tubes, or, better still, tubes fanned by cool air, are desirable.

If the *inductor apparatus* be used, the interrupter frequency should not exceed 30 or at most 40 per second. With the alternating current and *rectifying-switch apparatus* one uses the lowest number of impulses of which the machine permits.

The degree of *hardness of the tube* varies for different kinds of examinations. For röntgenoscopy of the lungs, a tube with a hardness of 8 Wehnelt nuits (half-value layer 1 cm.; 7 Walter units); for röntgenoscopy of the cardiovascular stripe, or of the gastro-intestinal canal, a harder tube is desirable (not less than 9 Wehnelt units; 1.2 cm. half-value layer; 7 or 8 Walter units). It is best to keep tubes of these strengths available, using the one strength for examining the lungs, and the other for the stomach and intestines. Used in this way, the tubes will last longer.

As to the *strength of the current* employed, 2–3 milliamperes will be sufficient with the inductor apparatus, 3–5 milliamperes with the alternating current and rectifying-switch apparatus.

The *Coolidge tube* is especially valuable for röntgenoscopy since the penetrability of the rays can be varied at will while the tube is in action.

The *direction of the transillumination* is varied according to the object in view. The following are the main directions:

1. *Sagittal direction.*
   (a) Dorsoventral (tube behind; fluorescent screen in front).
   (b) Ventrodorsal (tube in front; screen behind).
2. *Frontal direction;* that is, from side to side.
   (a) Dextrosinistral (tube on right side; screen on left).
   (b) Sinistrodextral (tube on left; screen on right).

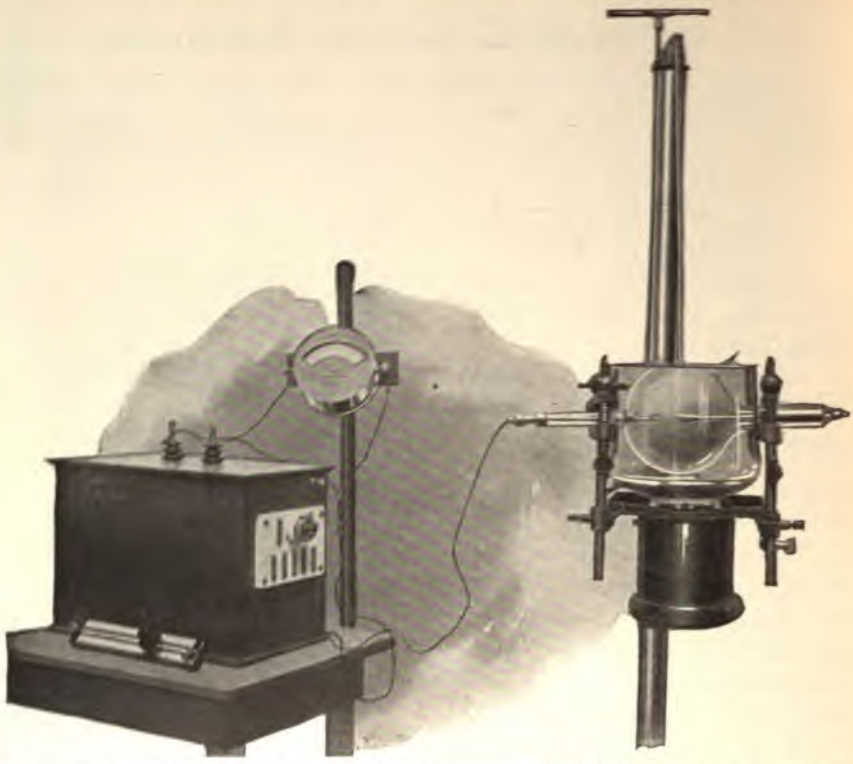


Fig. 23.—The Coolidge X-ray Tube, Operating in Connection with a Current Generating Unit for Heating the Cathode Spiral. The Amperemeter Indicates the Amount of Current Passing Through the Cathode Spiral of the Coolidge Tube. (By courtesy of the Kny-Scheerer Co.)

3. *First oblique diameter* (fencing position).
   (a) Dorsoventral (tube, posterolateral on the left; screen, anterolateral on the right).
   (b) Ventrodorsal (tube, anterolateral, on the right; screen, posterolateral on the left).
4. *Second oblique direction.*
   (a) Dorsoventral (tube, posterolateral on the right; screen, anterolateral on the left).
   (b) Ventrodorsal (tube, anterolateral on the right; screen, posterolateral on the left).

The examiner should remain at least 5 or 10 minutes in the dark room, until his eyes are perfectly adapted to the darkness, before making the examination.

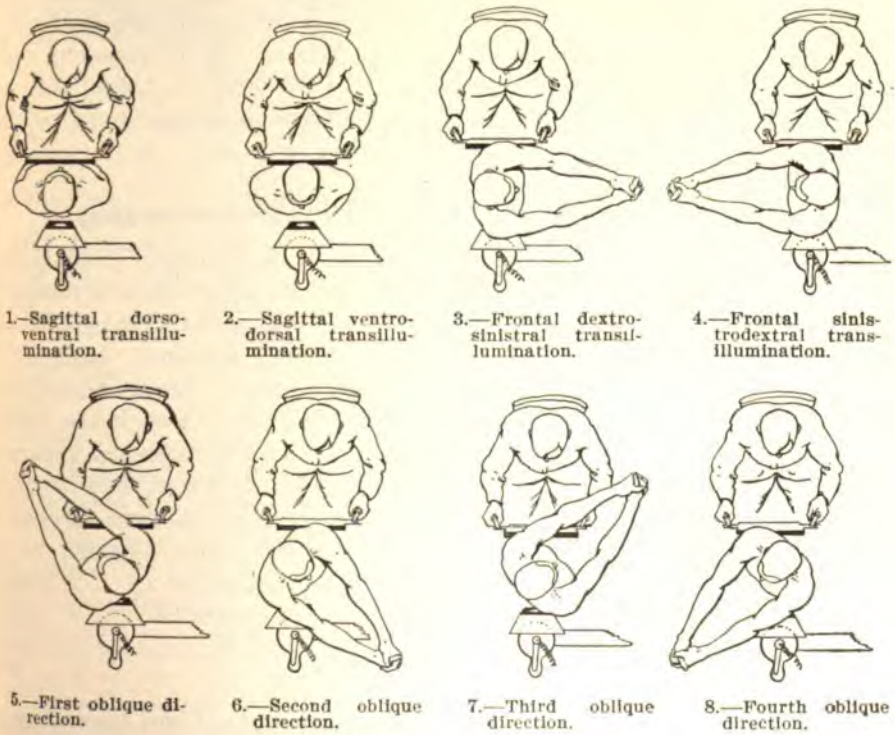
The application of röntgenoscopic methods to the thorax, heart, great vessels, trachea, lungs, diaphragm, esophagus, stomach, intestines, liver, and spleen will be referred to under the diagnosis of diseases of these several organs.

2. Technic of Röntgenography

Here a photographic plate takes the place of the fluorescent screen; after exposure, it is developed, fixed, washed, dried, and examined in a good illuminating box.

(*a*) *Maintenance of the Patient in Correct Position*

It is essential that the patient do not move during the exposure. Fortunately, with the alternating current and rectifying-switch apparatus, very short exposures are possible, and, with the single-impulse inductor apparatus, exposures of only 1/200 of a second suffice. Still, even with instantaneous exposures, it is necessary that the part shall stand in precisely correct relation to the pyramid of x-rays on the one hand, and to the photographic plate on the other; thus, whether the patient be standing, sitting, or lying, during the exposure, the exact position of the patient, and the maintenance of this, are of great importance. Supports of various sorts help to keep the patient in the correct position.



1.—Sagittal dorso-ventral transillumination. 2.—Sagittal ventro-dorsal transillumination. 3.—Frontal dextro-sinistral transillumination. 4.—Frontal sinistrodextral transillumination.

5.—First oblique direction. 6.—Second oblique direction. 7.—Third oblique direction. 8.—Fourth oblique direction.

Fig. 24.—Different Positions for Transillumination on Röntgenoscopy. (Redrawn after T. Brugsch and A. Schittenhelm.)

(*b*) *Compression Apparatus*

In making x-ray photographs of the kidneys, and sometimes of other parts, especially in stout individuals, it is helpful to use an *Albers-Schoenberg compression apparatus,* so as to lessen the body thickness; at the same time the x-rays are passed through a *ring,* or a *tube,* in order to avoid secondary radiation as much as possible.

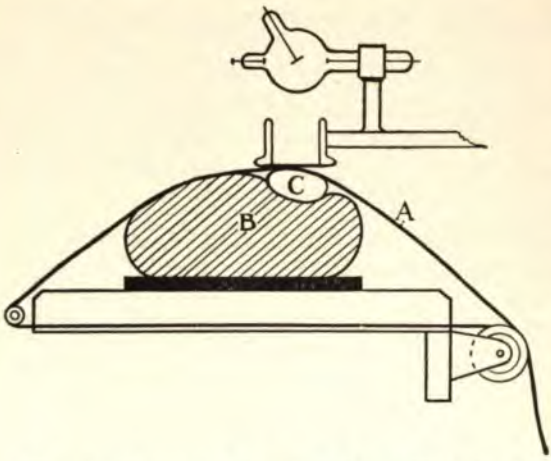


Fig. 25.—Compressor for Use in X-ray Work (Gurt).

More recently, the *Gurt compressor,* consisting of a broad band, pulled tightly across the body by means of a pulley and lever, permits of strong compression, without causing pain. Under the band, an air bag, or a cushion, may, if desired, be placed, in order to produce strong local pressure, for example, over one kidney.

It is common, nowadays, to combine some form of diaphragm, or tube, with the compression apparatus (e. g., *Lambertz's stand, Robinson's compression tube*).

(*c*) *Hardness of Tubes Used in Röntgenography*

For röntgenography, x-ray tubes of medium hardness (8–9 Wehnelt units; 1.2 cm. half-value layer; 7 Walter units) are employed, though for taking a hand, a foot, or the lungs, a somewhat softer tube will be used (6–7 Wehnelt units); while for photographing a kidney, harder tubes (7–7.5–8–9 Wehnelt units) are best. Still harder tubes are employed when photographing the passage of a bismuth meal through the stomach and intestine (9.5 Wehnelt units). With the rectifying-switch apparatus, softer tubes can be used with a higher intensity of current than is possible with the inductor apparatus; this accounts for the excellent results now being obtained in ordinary x-ray work. Indeed, on the average, one can use, with the rectifying-switch apparatus, a tube, softer by 1–2 Wehnelt units, than the tube required with the inductor apparatus.

(*d*) *Exposure Time*

This varies greatly, according to the end in view. Thus, *time exposures* last ten seconds, or a little longer, with a current of 2–3 milliamperes; *quick exposures,* last 1–10 seconds with a current intensity of 10–30–40

liamperes. *Instantaneous exposures,* with the strongest currents t the tube will bear, last from 1/20–1 second in the *slower instances,* 1/50–1/200 in the *quickest exposures* in which a single impulse is d. When making instantaneous exposures, an *intensifying screen* is ally placed over the dry photographic plate.

It is convenient to keep in mind the rule that, with all exposition-times, product (milliamperes of current × time in seconds) is about the same. e can, therefore, easily calculate the milliamperage that should be loyed with a given exposition time.

The following table, prepared by Janus and Schittenhelm, shows at a ace the exposition-time used for photographing the various parts of the y by means of the x-rays:

Synoptical Table of Exposition-Values for Different Parts of the Body (Janus and Schittenhelm)

of body of a medium ed adult (say 1,68 high; 70 kg. weight)	Focus-plate Distance	Hardness of Tube in Wehnelt Units					
		7	8	9	6	7	8
		Without Intensifying Screen			With Intensifying Screen		
		Exposition-value = milliamperes x seconds					
d, from in front.....	Tube-diaphragm, or 60 cm.....	...	350	**200**	120	**70**	40
d, from side.....	Tube-diaphragm, or 60 cm.....	...	250	**130**	70	**40**	25
and nose, lateral...	Tube.....	160	**100**	...	**35**	20	...
ical spine.....	Tube.....	**80**	50	...	**20**	...	...
acic spine.....	Tube or 60 cm.....	...	240	**130**	70	**40**	25
ax.....	60 cm.....	...	140	**80**	45	**25**	15
ax, lateral.....	60 cm.....	...	180	**100**	60	**35**	20
um.....	Tube.....	**200**	120	...	**40**	25	...
t and lungs.....	60 cm.....	80	**50**	30	15	**8**	5
t (distant view)....	2 m.....	...	200	**120**	...	**50**	25
lder.....	Tube.....	...	150	**90**	60	**35**	25
bar spine.....	Tube.....	...	400	**250**	150	**80**	50
bar spine, lateral...	Tube.....	...	...	**500**	...	**180**	120
um and coccyx.....	Tube.....	...	400	**250**	150	**80**	50
l, or vesical, stone..	Tube.....	550	**350**	...	**120**	70	...
ach and intestine...	60 cm.....	...	140	**80**	45	**25**	15
is, or hip-joint.....	Tube or 60 cm.....	...	400	**250**	150	**80**	50
.....	Tube.....	80	**50**	30	15	**10**	5
d.....	Tube.....	25	**15**	10	6	**4**	2
h or knee, from in nt.....	Tube.....	...	180	**100**	60	**35**	20
or knee, from side..	Tube.....	...	**140**	75	40	**25**	15
.....	Tube.....	100	**70**	40	20	**15**	10

The hardness of the tube most suitable for the various views is indicated by bold-face type.
The items given in the table hold only for work done with the best photographic appa- made for röntgenographic purposes.
The exposition-time can also be very well determined by means of a slide-rule (Fig. 25).

To use the above table of exposition-values, Janus and Schittenhelm give the following example: Let us suppose that it is desired to take a photograph of the stomach, for which a tube hardness of 9 Wehnelt units is best. On testing the tube, it is found that it stands well a current of 8 milliamperes. From the table, one sees that the *exposition-value* in milliamperes seconds is 80. If we divide this exposition-value (80) by the number of milliamperes (8), we see that the exposition-time necessary

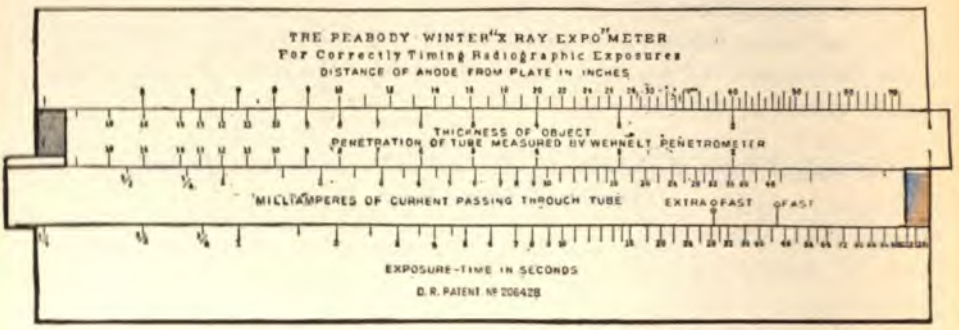


Fig. 26.—The X-ray Expometer. (By courtesy of the Kny-Scheerer Mfg. Co.)

(without intensifying screen) is 10 seconds. If, on the other hand, the instrument permits of a current of strong intensity, say 40 milliamperes, only 2 seconds exposure time will be required.

When using the intensifying screen, it is to be kept in mind that a tube, which has been measured with a current of 2–3 milliamperes, will be harder by about ½–1 Wehnelt units when a current of greater intensity (10 milliamperes and more) is passed through it.

(*e*) *Intensifying Screens*

An intensifying screen consists of a layer of calcium tungstate, which is laid over the photographic plate, in an especially constructed holder, or "kassette." Such a screen will shorten the exposure-time to 1/5, or even 1/30, of the ordinary time.

(*f*) *Special Clinical Applications of Röntgenography*

The special methods of applying röntgenography to the paranasal sinuses, the skull, the teeth, the lungs, the bronchial glands, mediastinal growths, esophagus, gastro-intestinal tract, gall stones, renal stones, vesical stones, bones and joints will be referred to under the diagnois of diseases of these parts.

(*g*) *Stereoscopic Röntgenography*

For the study of lesions in the lung (tubercles, cavities, pneumothorax), and for the study of the exact position of stones in the kidney, or

ureter, stereoscopic views are very helpful. In the clinic in which I work, Drs. Dunham and Boardman have made a large series of stereoscopic x-rays of the lungs. Another series, made by the röntgenologist to the hospital, Dr. F. H. Baetjer, in a number of normal people, has been controlled carefully by physical examinations made by Dr. Louis Hamman. We now have stereoscopic röntgenograms made as a routine in the clinic in the more interesting cases of intrathoracic lesion.

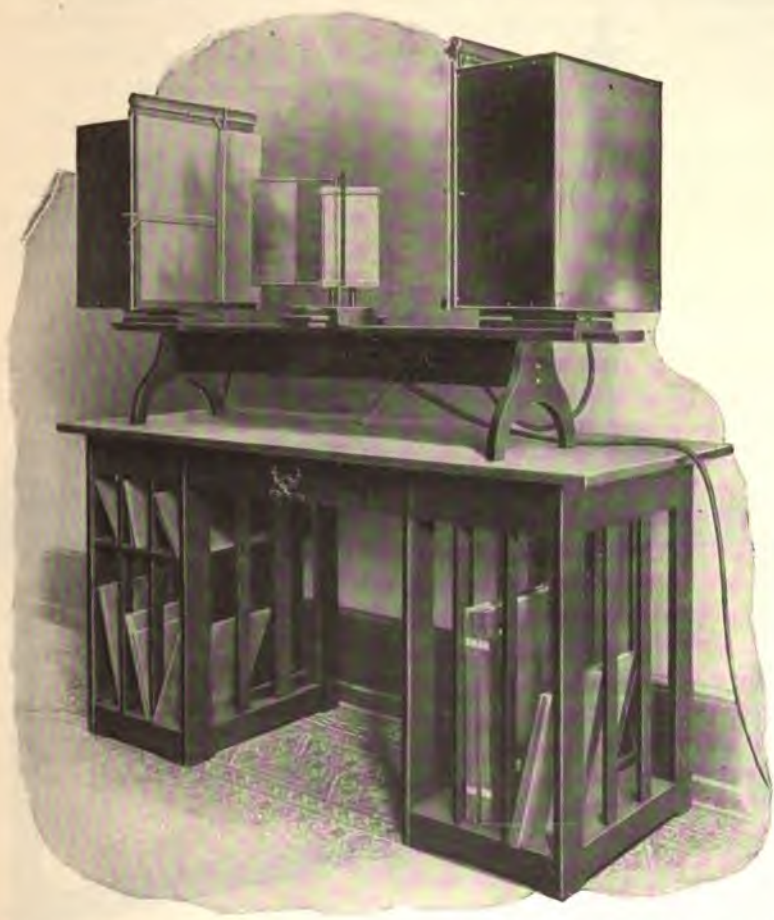


Fig. 27.—The Wheatstone Stereoscope. (By courtesy of the Röntgen Mfg. Co.)

These stereoscopic plates are indeed very instructive, and should be made in all cases where the diagnosis is difficult by ordinary methods. Two plates are exposed, without movement of the part photographed during, or between, the two exposures. The source of the x-rays for one plate must be 2½ inches away from the position of the source for the second plate (corresponding to the average distance between the centers of the two eyes). By

an ingenious arrangement, the x-ray tube is, therefore, moved 2½ inches between the two exposures, and the center of this line of movement is placed perpendicularly over the center of the plate. This movement of the source is accomplished by an automatic tube-shifting device. The vertical distance from the focus of the tube to the plate should be 14 inches plus the thickness of the object. The position of the vertical line, drawn from the focus-spot of the tube to the plate, is different for each of the two plates

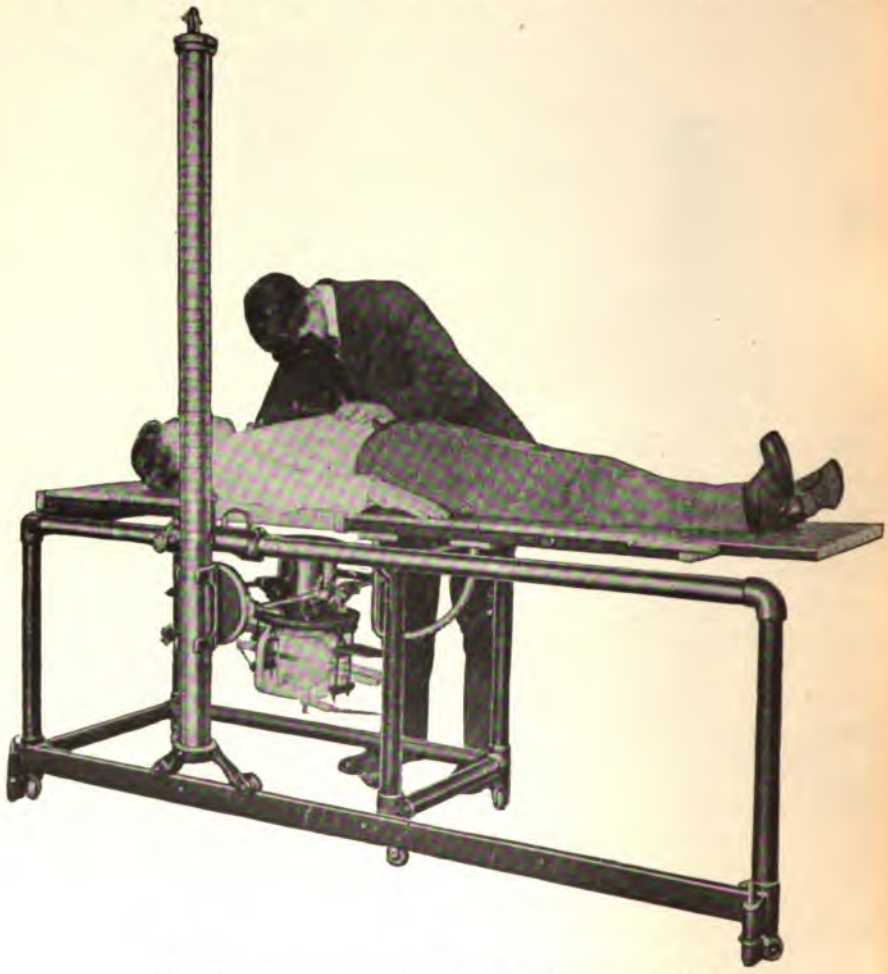


Fig. 28.—Röntgenoscopic Examination on Stereoscopic Table.
(By courtesy of Scheidel-Western X-ray Coil Co.)

because of the movement of the tube between exposures. The foot of the vertical line, at the point where it rest on the plate, is called the "foot-point" (Eijkmann). The operator marks the location of the "foot-points" on his finished plates; when viewing them, later, in the **Wheatstone**

stereoscope, he places them in the illuminating box, glass side out, and with the "foot-points" toward the back of the boxes. In viewing the plates in the stereoscope, the eyes of the observer must optically replace the focus-spots of the tube, in order to get correct impressions of depth without distortion.

Various plate-changing devices are used; these must support the object while the plates are being changed. Among them may be mentioned (1) the *non-automatic stereoscopic plate-changer;* (2) the *automatic stereoscopic tunnel plate-changer.* The latter shifts the plates in less than one second.

With the rectifying-switch form of apparatus, it is easy to make a pair of 14″ x 17″ chest plates in three seconds. The pulling of a cord releases the spring that shifts the plates.

In making stereoscopic röntgenograms of the kidneys, it is very convenient to have a **stereographic table** with automatic shifting apparatus and compression rings. Such tables are provided, also, with an inclined plane for frontal-sinus work.

(*h*) *Cinematographic Röntgenography*

Attempts have been made to prepare cinematographic films of moving organs in the body, photographed by the x-ray; thus, the shadows on a fluorescent screen have been directly photographed by an ordinary cinematographic apparatus, but unfortunately the yellow light of the fluorescent screen has very slight photographic effect. Cinematographic photographs have, however, been taken by this method of the internal organs of dogs and monkeys, the number of reproduction-pictures per second being exactly the same as the number of photographs taken.

Other workers, by means of a rapid plate-changing machine, have taken x-ray photographs on single plates, the x-ray tubes being excited synchronously with the change of plates, by means of the single-impulse apparatus. Thus far, it has not been possible to take more than 4 or 5 photographs per second by this method. Since to produce cinematographic effects, it is necessary to reproduce 15–18 pictures per second, these investigators have copied the picture from each single plate three or four times on the film, thus making the so-called *pseudo-cinematographic film* from the *kino-series plates* (Groedel; Rosenthal). Groedel of Nauheim has taken a kino-series simultaneously with electrocardiograms on which were marked, electrically, the times of the taking of the single röntgenograms.

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Part III

Exploratory Puncture and Examination of the Fluids Obtained

In this chapter we shall consider:

(A) The technic of exploratory puncture of the pleural cavity, pericardial cavity, peritoneal cavity and the subarachnoid space; and other exploratory punctures (liver, spleen, kidneys, joints, etc.) less commonly made;

(B) The examination by chemical and physical methods of the fluids obtained; and

(C) The examination by bacteriological, serological and cytodiagnostic methods of the fluids obtained.

A. The Technic of Exploratory Puncture

1. Exploratory Puncture of the Pleural Cavity

If we suspect the presence of fluid in the pleural cavity, and desire to inform ourselves, definitely, as to this point, we resort to exploratory puncture; we introduce a sterile needle into the pleural sac, and, if fluid is obtained, we investigate its nature.

Physicians are often too dilatory in resorting to the needle for differential diagnosis. Information regarding the pathological state and its etiology can often be more promptly and definitely obtained by exploratory puncture than in any other way, and the results may be highly important for therapy. At the same time, the clinician should not put in a needle before he has made a thorough examination by the ordinary physical methods. A careful physical examination will give the indication for the exploratory puncture if it exist, and will do much to prevent an unnecessary or a "dry tap." The most skilled physical examiner will occasionally be in doubt in making the differential diagnosis between pleural effusion,

lrawing it a little, the fluid will be obtained if any be present in
ral cavity in the region punctured. A thickened pleura may cause
y increased sense of resistance when the needle reaches it. Some-
uid will be found beyond such a thickened pleura.
ıe lung be penetrated, a little blood may enter the syringe. Usually
e of the lung is entirely harmless, and in pneumonia, where it is
e for serotherapeutic reasons quickly to establish the type of pneu-
s causing the inflammation, lung puncture may be resorted to for
ose if suitable sputum be unavailable (R. I. Cole).
dry tap result when the physical examination points strongly to
exudate, the needle should be removed and examined to make sure
it is not plugged, and (2) that it possesses good suction power; if
le be found to be working properly, the puncture should be repeated
jacent region. A dry tap is occasionally due to flocculi of fibrin in
.

of Pleural Puncture.—In choosing the spot for puncture, the clini-
l be guided by the physical signs, and, especially, by the presence of
If there be a flat area at the base, the puncture will be made
ere between the upper border of flatness and the level of the dia-
; since it is important not to injure the latter, it is a good rule not
ture at a level lower than that of the normal limit of the lung
nargin of the 7th rib in the right mammillary line; upper margin
h rib in the mid-axilla; upper margin of the 9th rib in the scapular

nterlobar empyema on the right side be suspected, a puncture in
rth space in the right axilla, is the site of predilection. The
ll is especially thin in the axilla. On the left side, on account of
tion of the heart, it is a safe rule not to puncture in front of the
axillary line. When fluid is free in the pleural cavity, puncture
capular line is best; but, when the exudate is encapsulated, one
when practicable, the center of the area of flatness.

oval of Large Amounts of Fluid from the Pleural Cavity.—For
pose an aspirator (Fig. 30) attached to a pleural trocar is best.
leural trocar consists of a cannula with a lumen of 2–4 mm.,
ith a sharp pyramidal stylet, which can be withdrawn after punc-
he pleural sac so as to let the fluid run through a lateral tube

the needle, (1) owing to the danger of injuring the lung; and (2) on account of the danger of inducing so-called albuminous expectoration by withdrawal of too much fluid; in the latter, the patient coughs up large quantities of frothy serum (danger of asphyxiation).

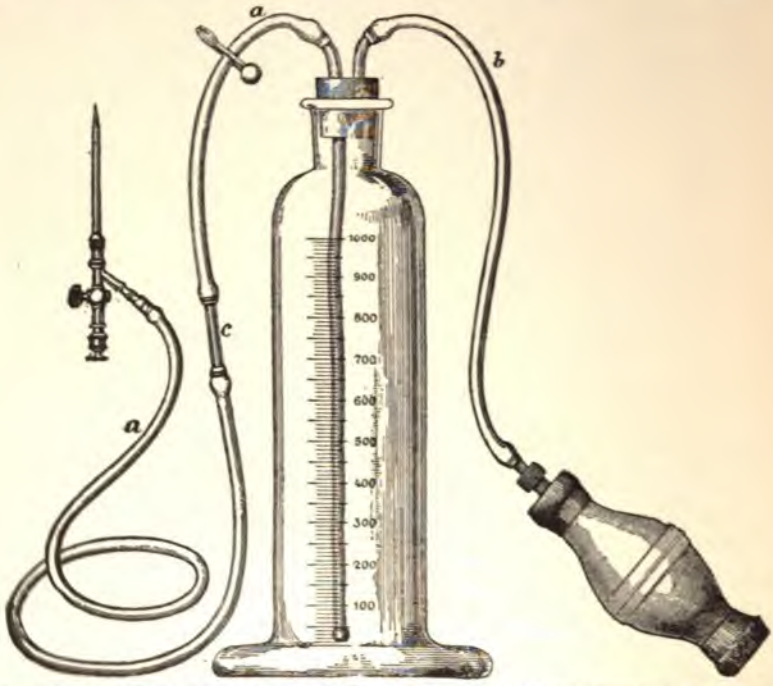


Fig. 80.—Thoracentesis Outfit. (After P. Krause, "Lehrb. d. klin. Diagnostik d. inner. Krankheiten," published by G. Fischer, Jena.)

If pus is present in the pleural cavity, removal by aspiration is insufficient, except perhaps in young children. Instead of aspiration, the pleural cavity should be drained by incision, and in most cases, to insure free drainage, a portion of a rib should be excised.

2. Exploratory Puncture of the Pericardial Cavity

This is resorted to when the presence of fluid in the pericardial cavity is suspected, and especially when the size of the exudate, or the course of the disease, makes removal of the fluid for therapeutic reasons seem advisable. The actual exploratory puncture determines the presence or absence of fluid, and, when fluid is present, its nature.

The skin is rendered aseptic with soap and water and with tincture of iodin, and the puncture is made with a Record syringe, as in the case of pleural puncture (*vide supra*).

In diseases ordinarily accompanied only by a serous or serohemorrhagic exudate, the determination of the nature of the fluid by puncture may not be important; but, in septic processes, the differentiation of a purulent exudate from a serous exudate in the pericardial cavity may be life-saving.

Having introduced the point of the needle well under the skin and then having withdrawn the piston so as to create a vacuum in the syringe, one pushes the needle slowly in until the fluid is reached and a drop or two begins to appear in the syringe. If the accumulation of fluid be considerable, the needle may be introduced in the 5th or 6th intercostal space, just lateral from the mammillary line, at a point beneath which there is absolute dullness but no pleural friction or cardiac pulsation. The needle should be directed obliquely inward and to the right, toward the apex of the heart. With this precaution, the heart will usually be avoided, but should the needle touch the apex of the heart, no harm is done as a rule.

If the accumulation of fluid in the pericardial sac be small, one may puncture in the 5th or 6th space on the left side, medial from the mammillary line, at the most lateral region of absolute dullness.

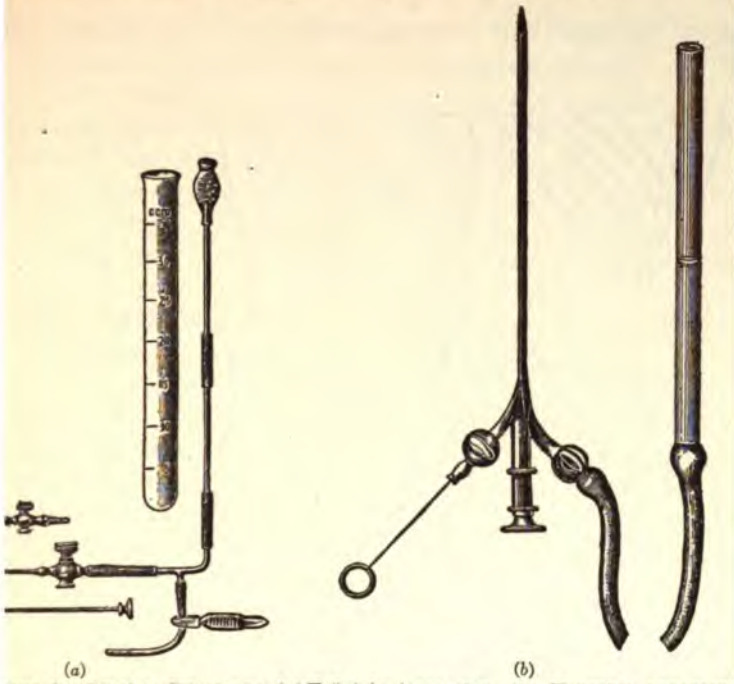
If the effusion be large, the needle may be introduced in the left costo-xiphoid angle, and be passed upward and backward, close to the costal margin.

3. Exploratory Puncture of the Peritoneal Cavity

If fluid be suspected in the abdominal cavity (ascites; inflammatory exudate), the physical examination may reveal shifting dullness in the flank, or, if the quantity be large, a fluctuation wave. When desirable to examine some of the fluid for diagnostic purposes, or if, for therapeutic reasons, the fluid should be drained off, we resort to abdominal tapping (*paracentesis abdominis*). The patient sits up in bed, most conveniently on the edge of the bed, the back being well supported by pillows or by an assistant. The skin is rendered aseptic (soap and water; tincture of iodin). Before tapping, one should make sure that the bladder is empty, passing a catheter if there be doubt.

The needle, or the trocar, is introduced in an area over which there is flatness or percussion, preferably in the middle line, a little below the umbilicus, or in the lower left quadrant at about the junction of the middle and lateral third of the line drawn from the umbilicus to the anterior superior iliac spine (avoidance of arteria epigastrica at the margin of the rectus abdominis). If a trocar be used, the puncture is made with the stylet in. When the peritoneal cavity has been entered, the stylet is withdrawn and the fluid allowed to flow out.

If a large quantity of fluid is to be removed, it is well to surround the



(a) (b)

ıtus for Lumbar Puncture: (*a*) Krönig's Apparatus, (*b*) Kausch's Apparatus
Krause, "Lehrb. d. klin. Diagnostik d. inner. Krankheiten," published by G
a.)

ture may be done with the patient either in the sitting posi
ıe lateral posture, lying on the left side, with the head and
nt forward
s drawn up
ıin, so as to
vidth of the
l spaces.
ı over the
e is thor-
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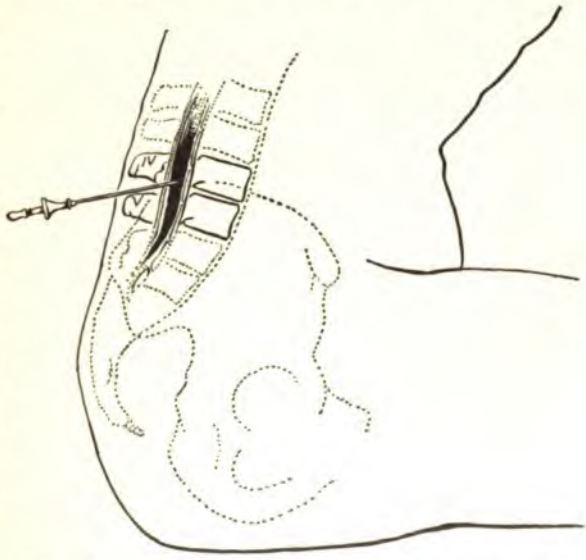


Fig. 33.—Lumbar Puncture. Introduction of the Needl
When the Patient is in the Sitting Position.

second and third, the third and fourth, or the fourth and fifth lumbar vertebrae. In the majority of cases, it is easiest to puncture between the third and fourth lumbar vertebrae. If one draws a line between the highest points of the two iliac crests, this line will pass through the spinous process of the fourth lumbar vertebra. The space above this spine is the one usually chosen for puncture.

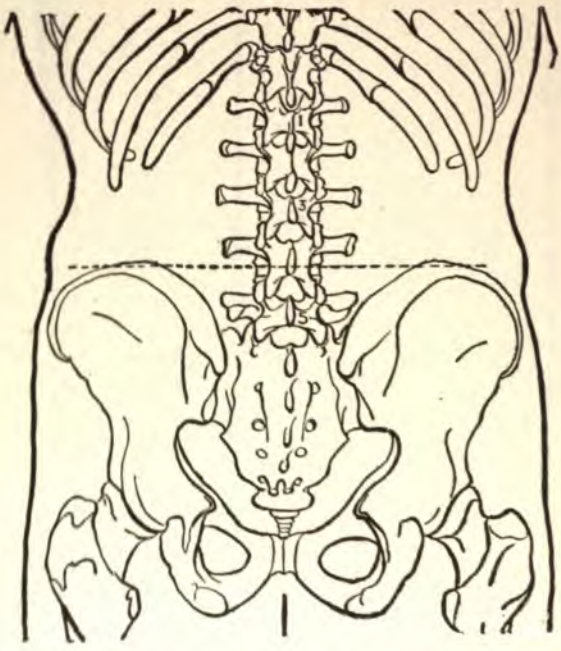


Fig. 34.—Selection of Point for Lumbar Puncture just above the Line Joining the Iliac Crests (in the 4th Lumbar Interspace) and Slightly Lateral from the Middle Line.

In children, the needle should be introduced exactly in the middle line, and should be directed almost straight forward, or a trifle upward; in the child, the needle passes 2 or 3 cm. into the depth before the subarachnoid space is reached.

In the adult, puncture in the middle line is the best routine procedure; it is sometimes easier however to introduce the needle at a point about 1 cm. lateral from the middle line at a level corresponding to the junction of the middle and lower thirds of the spinous process of the third lumbar vertebra. The needle is directed forward and medialward, so as to reach the meninges at about the middle line. In this way, the tough interspinous ligament is avoided. In the adult, the meninges lie 5–6 cm. from the surface; the needle must, therefore, be introduced for a distance of 6–7 cm. before the subarachnoid space is reached. After passing through the rather tough intervening tissue, the sudden letting up of the resistance announces the entrance of the point of the needle into the subarachnoid space.

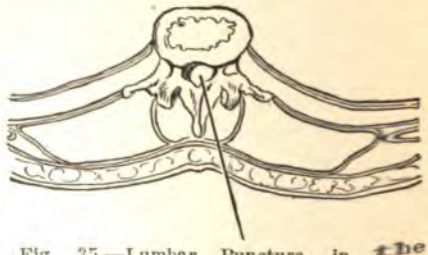


Fig. 35.—Lumbar Puncture, in the Adult. Note the Passage of the Needle Through the Soft Parts and the Interlaminar Space. The Needle has been Inserted Somewhat Lateral from the Median Line.

Since the spinal cord does not pass below the level of the second lumbar

ertebra, it cannot be injured by lumbar puncture. One might, of course, rike one of the nerves of the cauda equina, but this rarely occurs.

If the point of the needle be misdirected, it may strike against bone; this event it should be withdrawn a little, and the needle directed a little ore downward, as it is usually the bone above the space which is struck.

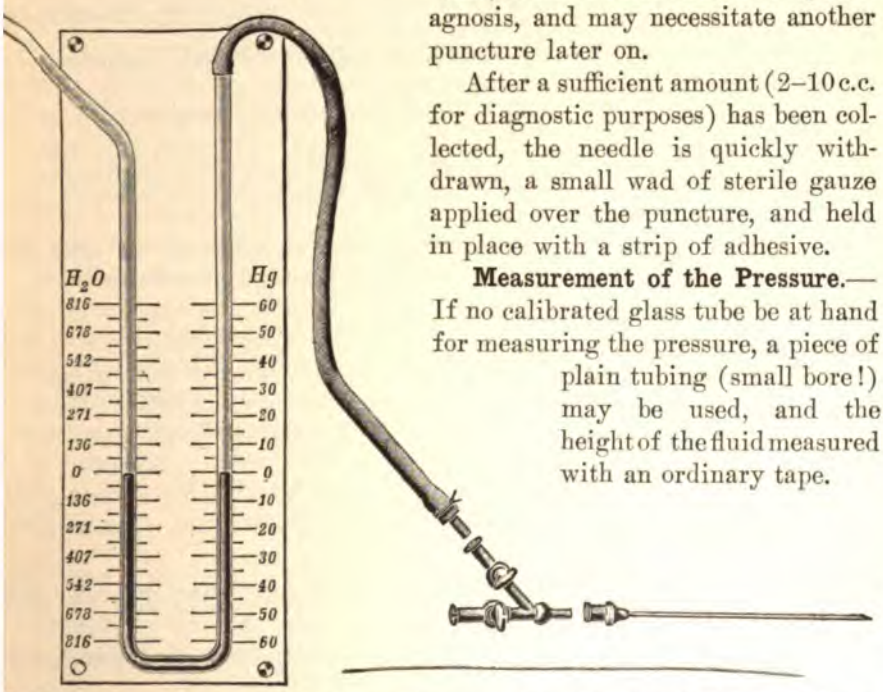
After the needle has reached the space, the stylet is withdrawn and the rebrospinal fluid appears, usually drop by drop. To measure the pres-re, the sterile glass and rubber tubing are immediately applied after thdrawal of the mandrin.

If the pressure is not to be measured, the fluid may be collected directly two sterile test tubes, say 2 c.c. in each.

Now and then, blood-tinged fluid is obtained. Occasionally, this is due hemorrhage into the subarachnoid space that has occurred before the ncture, but, as a rule, it is due to injury of a minute vessel at the time of ncture. This contamination of the fluid by blood is a regrettable occurrence, since it interferes with cytodiagnosis, and may necessitate another puncture later on.

After a sufficient amount (2–10 c.c. for diagnostic purposes) has been collected, the needle is quickly withdrawn, a small wad of sterile gauze applied over the puncture, and held in place with a strip of adhesive.

Measurement of the Pressure.—If no calibrated glass tube be at hand for measuring the pressure, a piece of plain tubing (small bore!) may be used, and the height of the fluid measured with an ordinary tape.



g. 36.—Manometer to be Used in Lumbar Puncture. The Scale gives the Absolute Value in mm., the Pressure Measured is Twice the Reading. (After E. Neisser, "Handbuch d. Neurol.," published by J. Springer, Berlin.)

The pressure of the cerebrospinal fluid under normal conditions corre-ponds to 40–100 mm. of water when the patient is in the recumbent posi-ion and breathing quietly. Before reading the pressure, one should wait until the patient is entirely quiet, since movements increase the pressure.

. Exploratory Puncture of the Skull Cavity (Neisser and Pollak)

method, considerably used in Germany, has not become popular in Amer-
e, we prefer exploratory puncture, after exposing the meninges by surgi-
tion like that used for decompression of the brain (Cushing). In Ger-
method is employed in suspected cerebral abscess, in hydrocephalus, and,
, in cases of tumor, or of cerebral hemorrhage. I regard it as an
ry and unjustifiable procedure.

6. Other Exploratory Punctures

ture of the *liver* may be necessary in the diagnosis of hepatic
or of echinococcus cyst (see Part VIII). As a rule, however, an
ry laparotomy is better.

ture of the *spleen* was formerly much used in the diagnosis of
It is rarely necessary, however, and is not devoid of danger.
opics, splenic puncture is often undertaken for the diagnosis of
(see Part IV).

ture of the *kidney* is sometimes undertaken for the purpose of
the contents of a cyst or an abscess. It is rare, however, that
neture is advisable (see Part X).

ture of a *joint-cavity* is sometimes undertaken for cytodiagnostic
riodiagnostic reasons, sometimes as a therapeutic measure. It
aseptically done, with a medium sized needle.

ture of a *lymph gland* may be necessary in the diagnosis of
sickness. Or a *bubo* may be punctured with bacteriodiagnostic
Bacillus of Ducrey; Treponema pallidum; Bacillus pestis).

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(c) *Specific Gravity of Punctates*

gravity of the fluid, as determined by an aërometer, is of distinguishing transudates from exduates. Most aërom- rated for fiuids having a temperature of 15–17° C. Since coagulate at these low temperatures, it is advantageous to calibrated for a temperature of 36° C. (Englander), and determination immediately after the withdrawal, using a ously warmed to a temperature of 36° C. in a water-bath. inary aërometer (standardized for 15° C.) is used when the the readings may be corrected by adding 0,001 for every 3° above 15° C.

tory exudates from the pleural cavity often have a specific 1018–1020, from the peritoneal cavity sometimes having a ity as high as 1030. Pleural transudates, on the other hand, lower specific gravity (1010–1015). In ascites, especially companying cachectic or hydremic states, the specific gravity late may fall as low as 1005.

ific gravity depends upon the quantity of substances in solu- ly, upon the amount of protein dissolved.

(d) *Protein Content of Punctates*

be roughly determined by Tsuchiya's modification of Esbach's the urine, diluting the fluid so that the reading in the Esbach less than 4, that is, so that the albumin content of the dilu- less than 0.4 per cent. We acidify the dilution slightly with and perform the test in the ordinary way (see Urine). The ade after 24 hours; if we multiply this by the dilution, the number of grams of coagulable protein per liter of punctate.

, rougher method still of estimating the amount consists in precipitate caused by a few drops of nitric acid added to the test tube. Thus, in inflammations, in tuberculosis, or in carci- pleura, the precipitate will consist of thick heavy masses of quickly fall to the bottom of the tube, while in transudates ardial insufficiency, the precipitate, still large, is looser and and in purely hydremic transudates, there may be only a escence, or small swimming flocculi (Runeberg).

exact determinations of the protein content, the total nitro- per cent is determined by Kjeldahl's method; then the non- gen is determined in grams per cent and subtracted from the multiplying the nitrogen value thus obtained by 6.25, we have n coagulable protein. The method is fully described by R. S. s made careful studies of the incoagulable nitrogen in punc- inds that in most punctates, the non-protein N is below 0.07

grams per cent. Values between 0.07 and 0.09 are of doubtful significance, but when the non-protein N exceeds 0.09 grams per cent, the probability is strong that the fluid is neoplastic in origin (cancer; sarcoma).

The protein content can also be determined by the gravimetric method:

1. Pour 10 c.c. of the punctate into 100 c.c. of boiling 1 per cent salt solution (feebly acidulated with acetic acid), and filter through a weighed filter.

2. Wash the coagulated protein on the filter with feebly acidulated water, and afterwards with alcohol and ether, and dry to constant weight at 100° C.

3. Subtract the weight of the filter and we have the protein content in 10 c.c. of the punctate; multiplying by 100, we have the protein content per liter.

In general, a high protein content (above 40–60 *g.* per liter) speaks for an exudate and low protein content (below 30 *g.* per liter) for a transudate; in stasis transudates the protein content varies between 10 and 30 *g.* per liter; in pure hydremic transudates it may fall as low as 1–3–5 *g.* per liter.

Rivalta's Test for Distinguishing Exudates and Transudates.—This is of some importance, since, in inflammatory exudates, the reaction is constantly positive, while in non-inflammatory effusions the test is entirely, or almost entirely, negative.

The test depends upon the presence in inflammatory exudates of a protein substance which is precipitated by acetic acid in the cold. In a glass graduate, or in a narrow beaker, one places 200 c.c. of distilled water and adds 2 drops of glacial acetic acid; to this feebly acidulated water a drop of the punctate is allowed to fall from a glass rod. If the substance on which the test depends be present, a gray cloud resembling tobacco smoke appears around the drop as it falls to the bottom. If only a minute quantity of the substance be present (as in transudates), this turbidity appears very slowly, and is much feebler. The nature of the substance concerned is in dispute (euglobulin and pseudo-globulin, globulin, or mucin?). Other methods of applying the test have been used by Runeberg, Umber, and Staehelin.

(e) *Freezing-Point (Molecular Concentration of Punctates)*

Cryoscopy applied to punctates is of but little clinical value, though it may sometimes be of interest to the scientific investigator. The method employed is that used in examining urine (q. v.).

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2. Cerebrospinal Fluids

(a) *Physical and Chemical Properties of Normal Cerebrospinal Fluid*

The normal cerebrospinal fluid is as clear as water, colorless, feebly alkaline, specific gravity 1008–1013, and with a protein content varying between 0.02 and 0.05 per cent. The sodium chlorid content varies normally between 0.55 and 0.8 per cent, the sugar content (determined with Haines's solution) between 0.06 and 0.09 per cent. The sugar disappears quickly on exposure to the air; it is supposed to be glucose (Kafka). The normal fluid contains a minute amount of cholin. The freezing-point is about the same as that of blood (—0.56 C.).

(b) *Physical and Chemical Properties of the Cerebrospinal Fluid in Pathological States*

In pathological conditions, the fluid may undergo important chemical and physical changes, though these are far less significant for diagnosis than the changes demonstrable by the methods of cytodiagnosis and of immunodiagnosis.

i. The Total Protein Content

The amount of albumin is increased in meningitis both in the acute, and in the chronic, forms. The total protein content can be approximately estimated by Tsuchiya's modification of Esbach's method, or, simply, by the heat and nitric acid test, more accurately by Kjeldahl's method or by the gravimetric method.

ii. The Globulin Content

Much more important for diagnosis, however, than the mere determination of the total protein content is the estimation of the content in globulin by methods introduced in 1903 in the French clinics (Widal, Sicard and Ravaut; Guillain and Parant) and subsequently improved by various workers. At first, the globulin was precipitated by magnesium sulphate, but later ammonium sulphate was found to be a more delicate precipitating agent. Among the methods now employed are those recommended (1) by Nonne and Apelt, (2) by Noguchi, (3) by Ross and Jones, and (4) by Pandy.

Nonne and Apelt Modification of the French Method.—Mix equal volumes of cerebrospinal fluid and of a neutral solution of Merck's ammonium sulphate (saturated with heat, filtered and cooled). This precipitates the globulin-nucleoalbumin

fraction within three minutes, and the precipitate is designated by Nonne and Apelt as *Phase I*, while the coagulable protein present other than globulin, obtained by boiling the filtrate from the preceding, is known as *Phase II*.

Both globulin and serum albumin are present in normal fluid in minute amounts; in pathological states, an increase in globulin goes approximately parallel to the total protein increase. The degree of increase, however, is more easily estimated for the globulin than for the total protein.

Normally, the globulin precipitate (Phase I) is seen only as a trace of opalescence. In such cases, Phase I is designated as negative. In the increased globulin reaction of pathological states we meet with several grades of globulin content, from (1) a trace of opalescence (normal), through (2) feeble opalescence, (3) opalescence, to (4) outspoken turbidity (Phase I, positive).

Phase I is never positive in functional diseases of the central nervous system. Even in lues, Phase I is negative unless the nervous system is involved. The method is strongly corroborative of the cytodiagnostic methods and of the Wassermann test in lues cerebrospinalis, in tabes, and in dementia paralytica.

In lues cerebrospinalis, Phase I is positive in the cerebrospinal fluid along with lymphocytosis of this fluid, though the Wassermann reaction in the fluid is usually negative, while the Wassermann reaction of the blood is positive (80 per cent of the cases). In general paresis, all four reactions are positive. An additional aid in distinguishing between lues cerebrospinalis and dementia paralytica lies in the colloidal gold test (see below).

Noguchi's Butyric Acid Test.—This is an excellent test for increased globulin, as those who have used it will testify.

1. Place 0.1 c.c. of cerebrospinal fluid in a test tube; add 0.5 c.c. of a solution of chemically pure butyric acid (10 per cent) in a solution of pure sodium chlorid (0.9 per cent); boil briefly over the flame of Bunsen burner.

2. Now add quickly 0.1 c.c. of N/1 sodium hydroxid; boil again for a few seconds.

If the globulin-content be increased, a coarsely granular, sometimes flocculent, precipitate will appear. It becomes visible, as a rule, within 10 or 20 minutes, but should none be visible at the time, the test tube is set aside for 3 hours, after which it is again looked at.

In normal cerebrospinal fluid, there is only a slight, even, opalescence; coarser precipitates never form, even if the fluid be allowed to stand for several hours after the test has been made. Simon Flexner has found the reaction very helpful in his experimental studies of cerebrospinal fluid.

If the character of the reaction be doubtful, a second test should be made, using 0.2 c.c. of fluid instead of 0.1 c.c.

Ross and Jones's Modification of the French Method.—This very delicate method is a favorite one with the assistants in the clinic. The same solution of ammonium sulphate is used as in the Nonne-Apelt method described above.

1. Place 2 c.c. of the solution of neutral ammonium sulphate in a test tube.

2. Incline the tube, and, with a pipet, allow 1 c.c. of c.s. fluid to run gently down upon the surface of the fluid in the tube, without mixing the fluids.

3. At the end of 3 minutes, examine the line of contact of the two fluids on

solution of formol (obtained by mixing 1 c.c. of commercial concentrated formaldehyd solution with 100 c.c. distilled water).

The gold sol should present a purple-red tone, and should be perfectly clear and transparent and remain free from sediment on long standing. In preparing the solution, and in carrying out the test, the greatest cleanliness must be observed.

Ten small test tubes are placed side by side in a test tube rack. In the first one is placed 1.8 c.c. of a 0.4 per cent solution of NaCl, and the amounts in each successive test tube increased successively by 1 c.c. of salt solution. To the first test tube is added 0.2 c.c. of the cerebrospinal fluid to be examined. From the mixture in the first tube one takes 1 c.c. and puts it into the second tube, and, after mixing, takes 1 c.c. from the second tube and places it in the third, and so on until one gets dilutions as high as 1:5,120. After these dilutions have been prepared, 5 c.c. of the gold sol are quickly poured into each tube and allowed to stand for a few hours, after which the reaction may be read off. A test tube with pure 0.4 per cent NaCl solution and 5 c.c. gold sol is used as a control; in this tube, the color must remain unchanged; otherwise the solution dare not be used.

Precipitates, and change of color, occur in various dilutions, according as the case is normal, or one of cerebrospinal lues, of tabes, of dementia paralytica, of meningitis, etc. It is customary to record the results in the form of curves.

It is too soon as yet to speak, finally, regarding the value of this gold sol test, but the studies of B. W. Sippy of Chicago, of Grulle and Moody in congenital lues, and of Sydney Miller of Baltimore, indicate that it may be of some value in the differentiation, especially of the different forms of luetic and para-luetic infections of the central nervous system.

[As this volume goes to press, a new article has appeared, in which Miller, Brush, Hammers and Felton describe (1) important modifications of the method of preparation of the colloidal gold reagent and (2) the criteria for judging the reaction; those who desire to use the method should consult this paper, the reference to which is given below.]

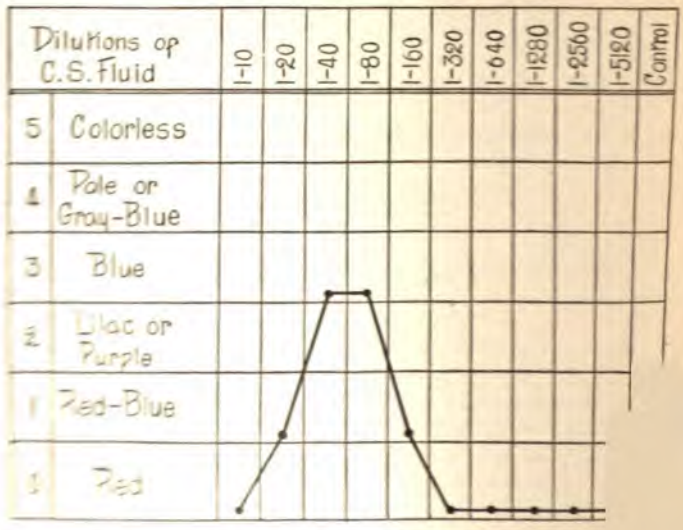

Fig. 3.—Diagram showing Numerical Values Assigned to Colors, and "Luetic Zone." (After Miller and Levy.)

PHYSICAL, CHEMICAL PUNCTATES

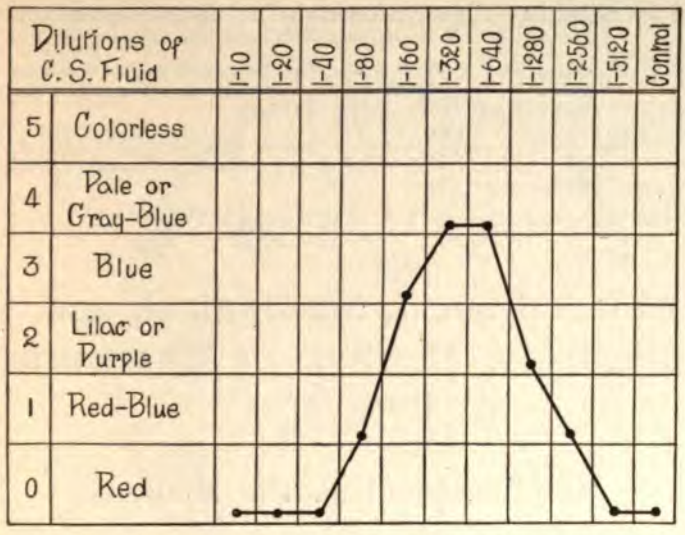

Fig. 38.—The Reaction in Meningitis. (After Miller and Levy.)

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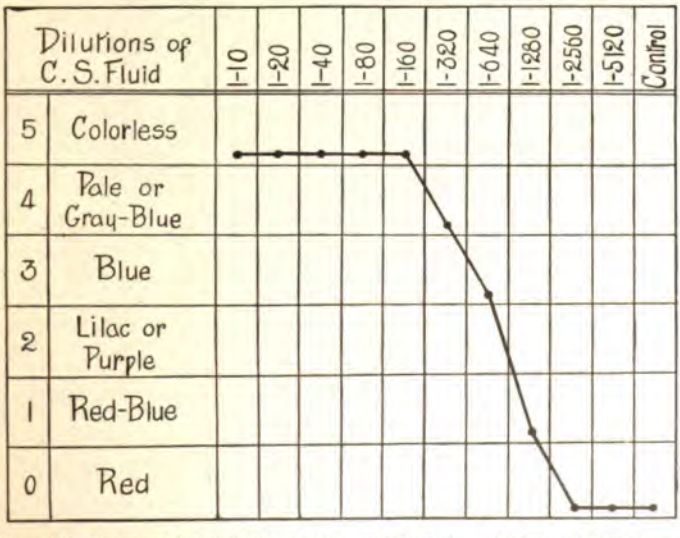

Fig. 39.—The Characteristic Curve of General Paresis. (After Miller and Levy

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[NOTE.—For other references on C. S. fluid, see end of Part IV.]

C. Bacteriological, Serological, and Cytodiagnostic Methods of Examining Punctates

1. Bacteriodiagnostic Methods

The methods described for making smear preparations, cultures on blood agar, and animal inoculations in the section on Infectious Diseases and on the Blood are applicable to the study of puncture fluids.

Tubercle Bacilli.—In fluids from the serous cavities and from the subarachnoid space, it is often desirable to search especially for *tubercle bacilli.* Formerly, exudates were subjected to artificial digestion **(inoscopy)** for this purpose. At present, we rely rather upon the **antiformin method,** in which the thick exudate or a sediment obtained on standing or on centrifugalization is mixed with 20–50 per cent antiformin, later centrifugalized and the sediment stained for tubercle bacilli.

In *tuberculous meningitis,* the cerebrospinal fluid collected in a sterile test tube may be allowed to stand for from 12 to 24 hours in the ice-box; at the end of that time, the delicate, filmy clot that forms may be spread out upon a glass slide, slowly dried in the air, fixed by passing through the flame three times, and then stained by the carbol-fuchsin method, in the ordinary way, for tubercle bacilli (J. Hemenway).

In *chronic cases of serous-membrane tuberculosis,* or of tuberculous meningitis, **inoculation of guinea-pigs** with 5–10 c.c. of the fluid may be employed for diagnostic purposes; it is best to inject the aseptically collected suspected fluid directly into the peritoneal cavity. At the end of three weeks, the animal may be killed, and the lesions may be examined histologically.

Other Parasites.—In the fluid obtained by lumbar puncture, **smears** of the sediment may be stained (besides for tubercle bacilli), for *meningococci,* for *pneumococci,* for *influenza bacilli,* etc., and in the tropics, where sleeping-sickness is suspected, for *trypanosomes.* In rare instances, it may be possible to find the *Treponema pallidum.*

PLATE I

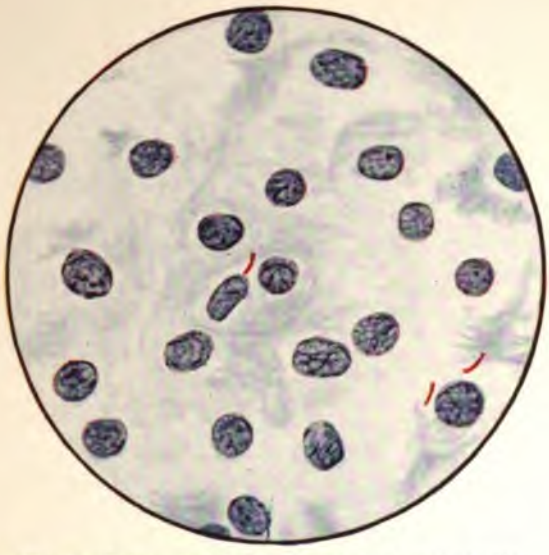

Fig. 1.—Tubercular Meningitis—Carbolfuchsin Methylene Blue. (After N. v. Jagic u. H. K. Barrenschen, "Atlas u. Grund. d. Klin. d. Mikroskopie," published by M. Perles, Wien.)

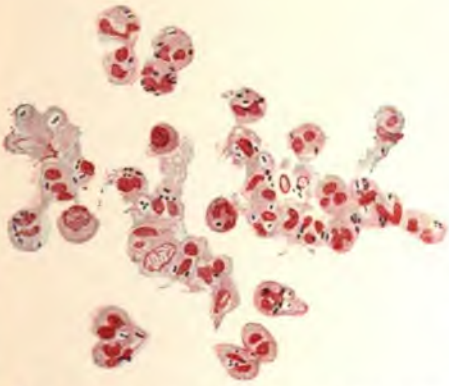

Fig. 2.—Diplococcus pneumoniae in Meningitis —Gram Stain. (After F. Plaut, O. Rehm u. H. Schottmüller, "Leitfaden zur Untersuch. d. Cerebrospinalflüssigkeit," published by G. Fischer, Jena.)

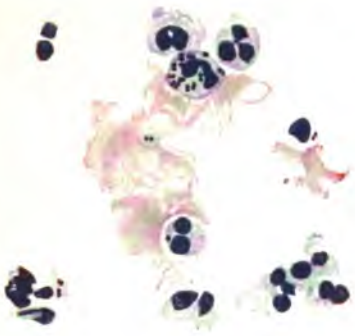

Fig. 3.—Meningococcus or Diplococcus meningitidis (Weichselbaum) in Cells in the Cerebrospinal Fluid. Stained with Methylene Blue. (After F. Plaut, O. Rehm u. H. Schottmüller, "Leitfaden zur Untersuch. d. Cerebrospinalflüssigkeit," published by G. Fischer, Jena.)

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2. Immunodiagnostic Methods

The most important of these for practical clinical purposes is the **Wassermann reaction** as applied to the cerebrospinad fluid. When the reaction is positive, we have the proof not only that the patient has had syphilis at some previous time, but that we have to deal, in the case before us, with some syphilogenous disease of the central nervous system (cerebrospinal lues; dementia paralytica; tabes). In *dementia paralytica,* the reaction is so constantly positive that a negative result almost rules out the disease. It is positive in 85–90 per cent of the cases if 0.2 c.c. of fluid is used, and in 100 per cent if 1.0 c.c. is used. In *tabes* the reaction is, in 90–95 per cent of the cases negative with 0.2 c.c. of fluid, but positive in nearly 100 per cent of the cases if 1.0 c.c. is used. In *cerebrospinal lues,* the reaction is also nearly always positive with 1.0 c.c., but negative in 90 per cent of the cases with only 0.2 c.c. of fluid. The reaction is usually positive in the blood serum in cerebrospinal lues and in dementia paralytica, but often negative in tabes.

The Wassermann reaction as applied to the fluid, when either positive or negative, should be accompanied by the results (1) of a Wassermann test applied to the blood serum; (2) of a test for globulin in the cerebrospinal fluid, and (3) of a cell count of the cerebrospinal fluid, in order that the best judgment possible can be formed regarding the underlying condition.

The technic of the Wassermann reaction is fully described in Part IV.

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3. Cytodiagnostic Methods

(*a*) *Cytodiagnosis of Pleural, Pericardial, and Peritoneal Fluids*

From the cytodiagnostic standpoint, four main types of these fluids are distinguishable: (i) exudates in acute infections of the serous membranes, (ii) exudates in tuberculous serositis, (iii) transudates, and (iv) effusions associated with neoplasms.

It is well to examine (1) a fresh unstained droplet of the sediment, and (2) dried and stained smears of the sediment. If the fluid be purulent, smears may be made directly from it; if it be clear, or turbid, it should be centrifugalized immediately after it is obtained, before clotting has taken place, or, if this be inconvenient, after treatment with an equal volume of solution of sodium fluorid (1 per cent), or a solution of sodium citrate (1.5 per cent) in physiological salt solution, when it may be kept without clotting and be sedimented, or centrifugalized, any time within the next 12 to 24 hours. Smears of the sediment are spread upon glass slides, air-dried, fixed and stained like blood-smears (see Examination of the Blood).

Unless the spinal fluid is purulent it is well to use some albumen-fixative on the slide before applying the stain. Otherwise it is common to wash the entire smear off. As a stain, we may use Jenner's, Wilson's, Giemsa's, or hematoxylin and eosin.

i. Cytodiagnosis of Exudates in Acute Infections

In the different forms of acute infectious serositis (pleuritis, pericarditis, peritonitis), aside from the demonstration in the stained smears, of the pyogenic microörganisms (streptococcus, staphylococcus, pneumococcus, etc.) concerned, one can often be fairly sure of the nature of the process by the large number of polymorphonuclear neutrophiles present. Occasionally, however, a primary tuberculous pleuritis may be ushered in by a temporary polynucleosis; but the degenerative changes that occur in the *polymorphonuclear leukocytes* representing the main contingent of cells in the exudate often suffice to differentiate the two groups of pleuritides. Thus the degenerative change in the pyogenic infections consists in a swelling and clearing up of the cell and of its nucleus, while in acute tuberculous pleuritis with polynucleosis, the cells are shrunken, and the nuclei pyknotic and fragmented (Koeniger).

In a few cases, large numbers of *eosinophils* have been met with in pleural exudates. Ordinarily, the eosinophils do not make up more than 1–4 per cent of the count, but in so-called "pleural eosinophilia," as many as 10–70 per cent of the cells may be eosinophils. The etiology appears to be variable.

When the cytological formula is lymphocytic, and not polymorphonuclear, it speaks strongly against an infection due to pyogenic microorganisms.

ii. Cytodiagnosis in Exudates Due to Tuberculous Infections

In tuberculous serositis, whether involving the pleura, the pericardium, or the peritoneum, there is often an outspoken *lymphocytosis* demonstrable in the fluid ("lymphocytic formula"). This may or may not be accompanied by the presence of *red blood corpuscles.* When the latter are present, also, the finding speaks strongly for a tuberculous etiology. In the beginning of an acute tuberculous pleuritis, a temporary polymorphonuclear leukocytosis may be demonstrable in the fluid. Even in outspoken lymphocytosis there may also be many polynuclears present, though the number is exceeded by that of the lymphocytes. But "tuberculous polynucleosis" can usually be distinguished from the polymorphonuclear formula in pyogenic infections by the behavior of the cells and their nuclei (see above).

In the more chronic forms of pleuritis, a lymphocytosis may be met with, not only in tuberculosis, but also in sarcoma of the pleura, and in luetic pleuritis. In the sarcomatous cases, however, many endothelial cells

accompany the lymphocytes; in luetic pleuritis, the Wassermann reaction is positive.

In instances in which polymorphonuclear cells predominate, the presence of a large number of lymphocytes (1/3 of the total count or more) and of red blood corpuscles should make one suspect a tuberculous etiology, especially if endothelial cells be absent, or present in only small numbers.

The study of the cells in exudates from tuberculous peritonitis yields findings resembling those in tuberculous pleuritis. There is always an outspoken leukocytosis, but the exudate differs from a pleural exudate in that there are, in addition, many large mononuclear cells and often many polymorphonuclears present. Endothelial cells may also be present in larger numbers than in the tuberculous pleural exudates. These endothelial cells are large cells with round or oval nucleus and a relatively large amount of protoplasm. The nuclei stain relatively feebly.

iii. Cytodiagnosis of Transudates

In simple hydrothorax, hydropericardium, and ascites, one finds, on cytodiagnosis, a very small number of cells, with preponderance of cells of the endothelial type, often united in chains or strips—the so-called "placards." Such *endothelial cells* may make up from 60-80 per cent of the total cell count. The remaining cells are chiefly lymphocytes, though, here and there, a polymorphonuclear element may be met with. Any circumstance that leads to a complicating inflammation of the serous membrane concerned will change the cell picture (appearance of polymorphonuclear elements).

iv. Cytodiagnosis of Effusions Associated with Neoplasms

These effusions are often rich in endothelial cells; occasionally, typical groups of *tumor cells* may be found in the fluid. If a minute fragment of tissue should be obtained, it is important to fix it, embed it, and section it, and then be guided by the histological picture found in the sections. Great care, however, must be exercised in asserting that a given cell is a tumor cell. Of course, if the cells are arranged in groups such as occur in known tumors, the diagnosis may not be difficult, but when one has to judge from single cells it is easy to err, though the so-called *seal-ring cells* with colloidal content and eccentric nuclei are characteristic, and, as Dock has emphasized, the presence of many cells containing nuclei undergoing karyokinetic division or mitosis, is very suspicious.

It should constantly be kept in mind also that a hemorrhagic effusion is in the majority of cases either of tuberculous or of neoplastic origin.

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(*b*) *Cytodiagnosis of the Cerebrospinal Fluid*

Here, the exact number of cells present as ascertained by a given method of technic is important in differential diagnosis. Two principal methods are employed:

(i) Counting and differential counting in stained smears, and (ii) the hemocytometer method of enumeration.

i. Counting and Differential Counting in Stained Smears

To estimate the number of cells in cerebrospinal fluid by this method, we centrifugalize 2–3 c.c. of the fluid for 45 minutes in a conical test tube, pour off the supernatant fluid, take up the sediment in a capillary pipet, mixing the cells well by blowing them gently back from the pipet into the tube, repeating this several times. A small droplet of the well-mixed sediment is then placed on a glass slide, spread out cautiously, dried in the air, fixed and stained. The earlier workers used a methylene blue stain. It is now customary to stain with Jenner's stain, or with one of the methylene-azure-and-eosin stains (Wilson's; Hastings's; Giemsa's).

Using a magnification of 300 diameters, and counting six fields of the microscope, the average number of cells in each field is then calculated.

The normal fluid should, according to Nissl, contain not more than from 4-8 cells in each microscopic field. If the number be 6-20 cells per field, Nissl speaks of *feebly positive* lymphocytosis; if the number be 20-60 cells per field, of *positive* lymphocytosis; if it exceed 60 per field, he speaks of *strongly positive* lymphocytosis; as many as 900-1,200 cells per field have been met with in some instances.

Obviously, for the enumeration of the cells in the fluid, such a method cannot be reliable. It is, however, of great value for the making of a differential count of the cells present, and the determination of the relative numbers (percentages) of the different varieties of cells (lymphocytes, polymorphonuclears, etc.) in the fluid. For making a differential count, it is desirable to count a large number of cells, 100–300 if possible.

ii. Hemocytometer Methods of Enumeration of the Cells in the Cerebrospinal Fluid

This is preferable to Nissl's method, and is the one used in the clinic in which I work. If it be associated with the study of a stained smear for the

differential count of the cells, it will be found very satisfactory. The exact number of cells per cubic millimeter of c. s. fluid is determined, very much as one counts the leukocytes in a counting-chamber. Either a Bürker modification of the Thoma-Zeiss cell counter with a Neubauer ruling (see Part VII) may be used, or, best, the Fuchs-Rosenthal counting-chamber.

Emerson's Method.—Into a "leukocyte pipet" of a hemocytometer, draw Unna's polychrome methylene blue as far as the mark 0.5; then draw in the fresh cerebrospinal fluid to the mark 11, or, if it be very rich in cells, to the mark 21. Mix well. Proceed as in counting the white blood corpuscles.

Rous's Method.—Into the "red corpuscle pipet" of a hemocytometer, draw a saturated aqueous solution of methyl violet (5 B), as far as 0.4 on the capillary tube; then draw in fresh cerebrospinal fluid, shaking thoroughly first to make sure that the cells will be evenly distributed throughout the fluid. Now mix the stain and the fluid, by holding the pipet horizontally, both ends closed, and shaking for three minutes. The counting-chamber of the hemocytometer is then filled, and the cells counted, just as in counting blood. The beginner should be careful not to count red blood corpuscles, should any be present, as lymphocytes.

Fuchs-Rosenthal Method.—The counting-chamber by this name is specially designed for the enumeration of cells in the spinal fluid; it is deeper and offers a larger ruled surface ($4 \times 4 \times 0.2$ mm.). Using a "white cell pipet" one draws in a staining fluid to the mark 1, and spinal fluid to the mark 11. All the cells in the entire ruled area are counted. The total number divided by 3 gives the number of cells per c.mm. An excellent staining-fluid has the following composition: methyl-violet 0.1, glacial acetic acid 2.0, water to 50.0. This fluid stains the nuclei and makes a differential count possible at the same time the enumeration is made.

If any hemorrhage has occurred in making the lumbar puncture and blood becomes mixed with the cerebrospinal fluid, it is best not to attempt a count of the cells. In such cases, it has been suggested that all the white cells (those of the fluid + those of the blood mixed with the fluid) be counted first; that then the red cells in the mixture be counted; that finally a red count and a white count of the patient's blood be made so as to determine the relative number of white and red cells in his blood; after this, a correction for the blood admixture with the fluid is made. But the sources of error are so great that I advise strongly against the use of this method. It is better to do lumbar puncture again later on and to examine a specimen free from blood.

In *normal cerebrospinal fluid,* the number of cells per cubic millimeter is usually less than 6; if more than 10 cells per cubic millimeter be found, the condition is to be regarded as pathological.

In addition to counting the cells, it is always well to make a smear from the sediment, and to dry, fix and stain this smear in order that the exact morphology of the cells (S. M.; P. M. N.; P. M. E.; P. M. B.; endo-

thelial cells; R. B. C.) may be studied and a differential count made (see above).

In the *various forms of meningitis,* the cell content of the cerebrospinal fluid is usually markedly increased. In *epidemic cerebrospinal meningitis,* polymorphonuclear cells predominate, though lymphocytes and large endothelial cells (some of them phagocytic) are also present. As the disease dies down, the polymorphonuclears decrease and the lymphocytes increase in number. A considerable lymphocytosis may persist for a long time after recovery.

In *purulent meningitis not due to the meningococcus,* but caused by pneumococci, streptococci, etc., the polymorphonuclears dominate the cell-count in the acute stage, though in convalescence lymphocytes appear.

In *tuberculous meningitis,* the lymphocytes are usually more numerous than the polymorphonuclear elements, though in some acute forms the polymorphonuclears may markedly predominate. With sufficient care, in such exudates, tubercle bacilli can usually be demonstrated.

In the *paraluetic* or *metasyphilitic* diseases of the central nervous system, there is an outspoken lymphocytosis of the cerebrospinal fluid. A careful study of smears shows, however, that, along with the lymphocytes, one may see large mononuclear elements, some polymorphonuclear cells, eosinophils, and endothelial cells; in other words, in such cases an actual **pleocytosis** exists. Such pleocytosis is found in every cases of *dementia paralytica,* though the cell-count may be low during remissions in the disease. In the majority of cases of *tabes,* also, a pleocytosis is demonstrable. In *cerebrospinal lues* (aside from tabes and dementia paralytica), the pleocytosis may be marked in meningoencephalitic or meningomyelitic processes; but the number of cells may be small in systemic degenerations of the white matter due to lues, in endarteritis, and in cases in which only isolated gummata occur (Lommel).

It should be remembered that a pleocytosis in itself does not permit us to separate luetic from metaluetic diseases of the central nervous system; moreover, a certain degree of pleocytosis may be met with in other chronic diseases of the central nervous system (*tumor; hydrocephalus; multiple sclerosis*). In *secondary lues* with skin lesions the cerebrospinal fluid may show an outspoken lymphocytosis, often in the absence of any other signs pointing to involvement of the central nervous system.

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Part IV

Diagnosis of the Infectious Diseases and of the Diseases Due to External Physical Causes

Section I

GENERAL DIAGNOSIS OF INFECTIOUS DISEASES

A. General Facts Regarding Infection, Infectious Processes and the Methods of Studying Them

1. Definition of Infection

By this term is meant the invasion of the body by living microörganisms, which find there conditions permitting of their multiplying and causing injury to the body, thus giving rise to disease-phenomena. Similar disease-phenomena sometimes follow intoxications in which no living parasites enter the body, e. g., after the ingestion of spoiled food (botulismus); here the microörganisms have produced outside the body the poisons that, when swallowed, give rise to symptoms. Many of the symptoms of diphtheria and of tetanus can be produced experimentally in susceptible animals by injection of their sterile toxins, but such toxins, unlike the microörganisms that generate them, are incapable of multiplication, and do not give rise in the animal to a communicable disease.

The *infectious diseases* (*morbi contagiosi*) were formerly subdivided into three groups:

(a) The *contagious* diseases proper, which are communicated from one person to another, either directly, or indirectly by objects (*fomites*) contaminated by a so-called "contagium";

(b) The *miasmatic* diseases, in which the infectious agent (*"miasma"*) enters the body from the outside, arising either independently of any sick person, or, if originating in another patient, undergoing some ripening process in the outside world;

(c) The *miasmatic-contagious* diseases, in which the infectious agent is supposed to go through two developmental stages before being capable of causing disease, one stage in a sick person, the other outside.

The artificiality of this classification has become obvious since the causes of the infectious diseases and the modes of their transmission have been worked out.

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2. Infectious Agents and Their Specificity

The agents that enter the body from the outside and are the "exciting causes" of the infectious diseases are minute living parasites (animal or vegetable), distinguishable from the non-pathogenic saprophytes by their ability to grow in higher living organisms and to injure such organisms.

The **vegetable parasites** belong chiefly to the (a) bacteria or fission-fungi (*Schizomycetes*), including the cocci, bacilli, and spirilla, though a few belong to (b) the *Trichomycetes*, including the leptothrix, cladothrix, and streptothrix forms and to (c) the *Blastomycetes* (or yeast fungi) and the *Hyphomycetes*.

The **animal parasites** causing infections belong to the protozoa, including (1) the *Rhizopoda* (e. g., amebae), (2) the *Flagellata* (e. g., trypanosomes), (3) the *Sporozoa* (e. g., coccidia) and (4) the *Infusoria* (e. g., balantidium).

The larger animal parasites like the parasitic worms (*Vermes*) and insects (*Arthropoda*) are not usually regarded as the cause of "infections" (due to microörganisms) but rather as the cause of "parasitic invasions."

Certain diseases (poliomyelitis, yellow fever, hydrophobia, etc.) are due to **filtrable viruses**, that is, to viruses that are so minute that they will pass through filters thought to be impermeable to ordinary bacteria; they are on the border line between the visible and the invisible, i. e., they are "ultramicroscopic."

Each infectious disease has a **specific cause**, that is to say, each infectious agent is capable of giving rise to a given disease; this disease can be caused by it alone, and the agent is incapable of transformation into one of another kind.[1] For example, the sore throat due to the diphtheria bacillus is a different disease from the sore throat due to the true streptococcus infection, though in many respects they may resemble one another clinically; again, a pneumonia due to the pneumococcus differs from a pneumonia due to Friedländer's bacillus.

Koch's Laws.—To establish beyond question the causal relationship of a given microörganism to a given disease, Koch required (1) that the suspected germ be present in all cases of the disease, (2) that its presence in the diseased tissues of the body be limited to this disease, (3) that it be grown in pure culture, and (4) that the disease be typically reproduced through inoculation of a healthy individual with the pure culture.

These requirements have been met for a few of the infectious diseases, notably for tetanus, diphtheria, pneumonia, and tuberculosis; but, for many of the infectious diseases, the first requirement only has been complied with. The causal agents in a large number of diseases, undoubtedly infectious in nature, are as yet

[1] Recent studies by E. C. Rosenow and by others hint that this specificity may not be so complete as we have been accustomed to believe. Thus Rosenow believes he can transform streptococci into pneumococci.

utterly unknown; this is especially true of the exanthemata (smallpox, scarlet fever, etc.).

For a time, medical men, delighted with their power to isolate the causes of some of the infectious diseases, were content to direct their energies largely toward such isolation as a means of diagnosis. More recently, since the essence of the infectious process has come to be recognized as a specific reciprocal influence—a kind of warfare—between the infectious agents on the one hand and the cells of the persons attacked on the other, interest has centered rather in the **mechanisms of aggression** and the **mechanisms of defense** of both parasites and hosts (*vide infra*). For the study of these mechanisms, the clinics and the experimental laboratories have employed the most diverse biological, chemical, and physical methods; these have led to the development of the elaborate technic which now characterizes the sciences of bacteriology, parasitology, and immunology.

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3. Mechanisms of Aggression of the Infectious Agents

(*a*) *Sources of the Infectious Agents*

The most important source is undoubtedly the sick man or animal, whence the germs may pass directly or indirectly to other men or animals and start new infections. It is, therefore, of the greatest importance to know (i) how the germs leave the bodies of the sick, (ii) how they maintain their existence, if at all, outside, and (iii) how they gain entrance into the bodies of other men or animals.

i. How the Germs of Disease Leave the Bodies of the Sick

This varies for the different diseases and their respective infectious agents. The germs may leave:

1. Through the *feces* (typhoid, cholera, dysentery).
2. Through the *urine* (typhoid, Malta fever, bubonic plague, tuberculosis, etc.).
3. Through the *saliva* (hydrophobia).
4. Through the *milk* (tuberculosis, anthrax).
5. Through the *sputum* (tuberculosis, pneumonia, diphtheria, streptococcus infections, influenza, plague, etc.), especially through the spray during speaking, coughing, and sneezing in the so-called "droplet-infection" (Flügge).

6. Through *pus* and through the *secretions* of the diseased skin and mucous membranes (gonorrhea, lues, tuberculosis, meningitis, poliomyelitis, exanthemata), and, perhaps, by scales of the skin itself (scarlet fever?).
7. Through the *blood,* by means of insect bites, or by transfusion (malaria, yellow fever, sleeping sickness, relapsing fever, typhus).

ii. How the Germs of Disease Maintain their Existence Outside the Bodies of the Sick

Certain germs (e. g., malarial parasites) seem to be incapable of living outside the body of some animal, *except under very special (artificial) conditions.* Others are capable of existing for a shorter or longer time in the outside world under natural conditions, provided they find sufficient nourishment and conditions not too inimical to them (drying; sunlight).

Some germs are not readily killed by drying, and so may be spread through **dust** (e. g., tubercle bacillus, pyogenic cocci, tetanus bacilli, anthrax spores, etc.); others are not viable in air-dried dust (gonococcus, influenza bacillus, cholera vibrio, plague bacillus).

Some germs can live in **water** under natural conditions for some time, even for weeks or months. Much typhoid fever, cholera, amebic dysentery and bacillary dysentery is due to water-borne infection. Polluted waters may contaminate oysters or shell fish with typhoid bacilli or with cholera vibrios. Freezing does not kill the cholera vibrio, so that ice may be a source of infection.

In **soil,** though the deeper layers are sterile, certain germs, notably those of typhoid and cholera, may be viable for some time. Anthrax bacilli assume the spore form and live for some time in soil. In manured soils, such as garden earth, tetanus bacilli and gas bacilli may remain viable for a long period.

Various **foodstuffs** may harbor pathogenic germs, either through their direct derivation from diseased animals (tuberculosis, anthrax, Malta fever), or through contamination on the way to the consumer (milk, meat, fish, oysters).

Certain *healthy human beings and healthy animals* may harbor pathogenic germs and not be ill themselves. These are the so-called **healthy carriers,** who play, perhaps, an important part in the spread of typhoid fever, cholera, diphtheria, influenza, meningitis, poliomyelitis, and plague. Again, certain pathogenic bacteria are capable of living in the skin (staphylococci), mouth, and throat (pneumococci; streptococci), or digestive tract (B. coli; streptococci) of most healthy human beings; under certain special conditions these germs may infect the carrier himself. Certain animals act as mechanical carriers of germs; thus flies may carry typhoid bacilli to food or directly to the lips of human beings.

Among the most interesting modes of life of germs outside the bodies of the sick is life in an **intermediate host** in which a developmental cycle necessary for the acquisition of the power to infect is gone through (parasite of Texas fever in the tick; malarial parasites in the anopheles mosquito; virus of yellow fever in the stegomyia mosquito).

iii. How the Germs of Disease Gain Entrance to the Body (Portals of Entry)

In the infectious diseases, the germs enter the body through one or another opening—the so-called "portals of entry." As long as the epithelium of the skin and of the mucous membranes is absolutely intact, infection does not occur through them, but should the epithelium be physically or chemically injured (wounds, heat, poison), germs may penetrate, and, multiplying within the tissues, start an infectious process.

Among the **portals of entry** may be mentioned the skin with its gland ducts and hair follicles, the conjunctiva, the nose, nasopharynx, and paranasal sinuses, the mouth (especially the gums), the tonsils, the bronchi and pulmonary alveoli, the mucous membrane of the esophagus, stomach, and, especially, of the intestine (including the bile ducts, pancreatic ducts, and vermiform appendix), the anus, especially when hemorrhoids or fissures exist, and the urogenital tract (including the urethra, bladder, ureters, and renal pelves in both sexes, and the mucous membranes of the special organs of sex in the male and in the female).

By **germinal infection** is meant the transmission of infection to the child by means of the egg cell or the sperm cell of a parent. Syphilis may be thus transmitted, but placental infection from the mother is probably more frequent than direct germinal transmission. Intra-uterine (placental) infection may occur in a number of diseases (e. g., syphilis, typhoid fever, tuberculosis, smallpox, etc.).

Certain germs can enter through almost any portal, while others never enter the body except through a single portal. Thus, plague bacilli may enter through the skin, through the mouth, through the lungs, or through the conjunctiva. But, as far as we know, the cholera spirillum acts only upon the intestinal mucous membrane; injected under the skin it does not cause disease except in the rare instances in which the cholera vibrios wander thence to the intestine. Midway in position between the organisms which can enter by almost any portal and those limited in entrance to a single portal, are the germs that, while preferring definite portals, occasionally enter through others. The bacillus of diphtheria preferably attacks the mucous membrane of the throat, but occasionally it may attack the nose, the conjunctiva, or the larynx. It rarely, if ever, attacks an open cutaneous wound. Similarly, gonococci preferably attack the urethral mucous membrane; but they may invade the rectum or the conjunctiva; they do not multiply in cutaneous wounds.

The *number of germs gaining entrance* may be of great importance. If only a few enter they may be quickly overcome before they give rise to evi-

dent signs of disease. In experimental animals, the number necessary to give rise to a fatal infection is known as the "minimal lethal dose."

Occasionally, more than one infectious process is going on in the body at the same time. If the two infections arise simultaneously we speak of **mixed infections**; if one follows upon the other we speak of a **secondary infection**.

Such contemporaneous infections are often important clinically. Many of the deaths in diphtheria and scarlet fever are due to complicating streptococcus infections. A terminal septic infection in typhoid is not uncommon. The streptococcus and influenzal infections complicating pulmonary tuberculosis are well-known and much feared.

(*b*) *Distribution of Microbes Within the Body After Entrance*

In certain of the infectious diseases (diphtheria; tetanus), the germs remain at the portal of entry, or extend along the contiguous surface, without going far into the tissues, and without being disseminated through the blood or lymph to distant points; these are **local infections.** The action of the germs themselves in such instances is purely local, but they often injure distant parts of the body through the production of soluble poisons, which are absorbed. Such diseases are often spoken of as **intoxication diseases** in contrast with the infectious diseases in the narrower sense in which the germs reach various distant points of the body by **metatasis** through the blood or lymph (e. g., infectious polyarthritis), or on entering the blood or lymph, multiply there in large numbers, giving rise to septicemia or **bacteriemia** (e. g., anthrax).

In some diseases, bacteria may, after a period, cease to multiply, but some of them may still remain alive in secluded parts of the body (**latent infection**), and under special circumstances, later on, begin to multiply again with renewal of disease symptoms. Such latent infections are especially common in the protozoan invasions (lues, malaria, trypanosomiasis), but latency is also met with in bacterial diseases (e. g., erysipelas, subacute infective endocarditis, chronic polyarthritis, tuberculosis).

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(*c*) *The Poisons (Toxins) Produced by the Microbes, and Their Action*

These are divisible into two groups: (1) soluble substances which may be looked upon as metabolic products or secretions of the germs—the so-called **ectotoxins** (e. g., the toxins of tetanus and diphtheria), and (2) poisonous substances contained within the bodies of the bacteria themselves

and set free only when the bacteria are broken up—the so-called **endotoxins** of Pfeiffer (e. g., the poisons derived from the bodies of pneumococci, tubercle bacilli, typhoid bacilli, cholera vibrios, etc.).

A number of other poisons should be mentioned here. The so-called **ptomains** are substances derived from the nutrient media in which bacteria grow. They resemble alkaloids and their nature depends upon the individual species of microörganism taking part in the process and upon the nutrient medium invaded (meat, cheese, ice cream, etc.).

The **bacterioproteins** of Buchner are thermostable proteins derived from bacterial bodies. These proteins are usually pyogenic in action when injected under the skin. Those from different bacteria resemble one another closely. Old tuberculin and mallein are rich in such proteins.

The nature of the so-called **aggressins** of Bail is still disputed. Bail believes that bacteria produce aggressins that paralyze phagocytes, since bacteria injected into animals along with the sterilized exudate produced by infection with the same bacterium kill more quickly than when the bacteria are injected without such exudate.

According to an hypothesis of W. H. Welch, bacteria may be stimulated by their host to the production of **bacteriogenic antibodies** that exert a specific toxic effect upon the cells of the body of the host—a bacteria-protective mechanism on the part of the bacteria to overcome the bacteria-offensive mechanisms of the body.

Certain other chemical substances produced by the germs in the body (especially the **antigens** that give rise to precipitins, agglutinins, opsonins, and lysins) will be referred to further on when the phenomena of immunity are discussed.

Selective Action of Poisons.—The poisonous substances produced by the germs often exert a selective action upon the various parts of the body. Certain organs possess an especial affinity for certain poisons. This has been shown in the test tube, notably for the tetanus toxin, which is avidly bound by fresh emulsions of cerebral gray matter. Similarly, the laking poison produced by staphylococci, and known as staphylolysin, is quickly bound by red blood corpuscles in test tube experiments.

Union of Poisons with Body-Cells.—One difference between susceptible animals and those that are insusceptible to a given infection seems to consist in the capacity of certain body-cells to unite with the poisons produced; thus, tetanus toxin injected into susceptible animals disappears from the blood in from 4–8 minutes. Injected into lizards, the toxin is demonstrable in the blood for two months, though the lizard shows no symptoms. It has no cells, apparently, which unite with the toxin. A scorpion injected in the same way shows no symptoms, though the toxin quickly disappears from the blood; in this animal it unites with the liver cells and can be again extracted from the liver, the extracts producing typical tetanus in mice.

Distribution of Poisons in the Body.—In the distribution of poisons in the body and their retention in certain organs, physical conditions such as solubility-relations are in part responsible and chemical affinities also play a rôle.

Poisons, while usually disseminated through the blood current or the lymph stream, may in certain instances follow a wholly different route; thus, in tetanus, the toxin reaches the central nervous system neither by way of the blood nor of the lymph, but, entering the motor nerves at the myoneural junction, travels in a centripetal direction until the central nervous system is reached.

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(*d*) *The Course of an Infectious Process*

Some little time elapses after the microbes have gained entrance into the body before the first symptoms of the disease appear. This time is called the period of **incubation.** Usually the outspoken symptoms of the disease are preceded by a brief stage in which there are more or less vague symptoms (*prodromata*). Before recovery from an infection, there may be one or more periods of exacerbation, often spoken of as a **recrudescence** or an intercurrent relapse. Sometimes the infection appears to have been entirely overcome and convalescence fully established when the patient and the physician are surprised by a recurrence of the symptoms of the infection; such a condition is called a true **relapse** or recidive.

(*e*) *The Virulence of the Microbes*

A microbe is said to be pathogenic, or virulent, when it is able to multiply in the organism invaded and to produce poisons that injure it. The degree of virulence varies according to the extent of these two capacities.

Virulent organisms often become avirulent when grown upon artificial media. Sometimes the virulence can be renewed by passage through susceptible animals, the virulence increasing on passage from one animal to another until a maximum is reached, the so-called "fixed virus" of Pasteur.

As the microbes grow more virulent, they acquire increased resistance to the antibodies produced by the organism invaded, and become less susceptible to phagocytosis. In addition, the microbes may produce substances (bacteriogenic antibodies) that combat the chemical agents used by the organism invaded in its defense (Welch).

Despite the increase in virulence of microbes by experimental passage through susceptible animals, virulence remains at a relatively low level in nature, and the mortality rates of infectious diseases appear to be falling rather than rising. A plausible biological explanation has been given by Theobald Smith, who suggests that many pathogenic microbes are being reduced to a more parasitic form of life. A microbe, to maintain its existence, must be able to adapt itself to conditions that allow the invasion of host after host. In addition, the most susceptible hosts are being gradually weeded out. The advance toward parasitism on the part of the microbes and the advance toward less susceptibility on the part of the hosts must be followed by a decline in virulence and in mortality rates.

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4. Mechanisms of Defense of the Human or Animal Body

Though an infected animal supplies a nutrient medium for the growth of the invading microbe, it possesses manifold **mechanisms of defense**, which it makes use of in repelling, or in overcoming, the enemy. When we consider the variability of the pathogenicity and virulence of the microbes on the one hand, and the variability in the susceptibility and in the mechanisms of defense of the hosts on the other, we can understand why the symptoms and course of infections must vary, and how unlikely it is that a given concrete case under observation will conform in every particular to a "typical text-book description."

When a person is protected by natural or artificial means against a certain infection or intoxication, he is said to be **immune**. When he is not so protected he is said to have a disposition for, or to be **susceptible** to, the disease.

(*a*) *On Immunity in General*

Inborn protective power of the organism against infections is known as **natural resistance** or inborn immunity. The protective powers that are acquired in the course of life are spoken of as **acquired immunity**. It has long been known that one attack of certain infectious diseases protects from subsequent attacks. The acquired immunity here is natural, or spontaneous, but in many instances we can produce an immunity at will, by systematically treating the body with the microbes or their poisons (*active immunization*). These harmful substances, known as antigens, give rise to reactions in the hosts that lead to the production of so-called antibodies that neutralize or destroy the antigens.

In acquired immunity, the protection may depend upon the chemical neutralization of pathogenic toxins by specific antitoxins **(acquired antitoxic immunity)**. In some instances it may depend upon the acquisition of the power quickly to destroy the entering microbe **(antibacterial or bacteriolytic immunity)**; in still other cases the protection may depend upon the formation of substances that prepare the bacteria for phagocytosis **(phagocytic immunity)**. Immunity may also be produced by injecting immune substances derived from artificially immunized animals (*passive immunization*).

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(*b*) *Natural Immunity, or Resistance*

This may be either antibacterial or antitoxic.

i. Antibacterial Resistance

An antibacterial resistance may depend upon (1) the closure of the portals of entry, (2) conditions unfavorable to the growth of bacteria after entrance, or (3) bactericidal powers of the fluids themselves.

Natural bactericidal action of the blood depends upon substances in the serum **(alexins)**; these are thermolabile and resemble ferments in that they require a certain temperature, a slightly alkaline or neutral reaction, and a certain salt content, to exert their bactericidal effects. The serum can be made inactive by heating thirty to sixty minutes at 55° to 60° C., which destroys the alexin. In acquired bactericidal action of the blood, other substances are important. (See Bacteriolysis.)

In **phagocytosis,** the microbes are taken up by the cellular elements and undergo digestion inside them. In human beings, it is the mesodermal element and especially the white blood corpuscles and the endothelium of blood and lymph vessels, which act as phagocytes. The polymorphonuclear leukocytes have been designated *microphages,* while the large mononuclear cells, the large lymphocytes, the giant cells, and the pulp cells of the spleen and bone marrow are called *macrophages.* Most microbes are taken up by microphages, but the tubercle bacillus, the actinomycosis fungus, and animal parasites are more often engulfed by macrophages.

The phagocytes are peculiarly susceptible to chemical stimuli **(chemotaxis).** Certain chemical substances of bacterial origin attract leukocytes

to them in large numbers. They are *positively* chemotaxic. Other substances appear to drive leukocytes away from them. They are said to be *negatively* chemotaxic. A third group of substances neither attract nor repel the phagocytes. They are the so-called *indifferent* substances. A given substance may be positively chemotaxic in one concentration, and negatively chemotaxic in another. It seems probable that the leukocytosis and the leukopenia met with in the infectious diseases are in part to be explained upon a chemotaxic basis; in addition, stimulation or depression of the leukopoietic tissues must also be considered. (See Leukocytosis and Leukopenia).

Both non-virulent and virulent bacteria may be engulfed by phagocytes. Usually the bacteria undergo intracellular digestion and destruction, but virulent microbes may remain alive and retain their virulence for a long time within phagocytes.

It was formerly thought that substances exist in the serum that stimulate the phagocytes to activity. They were called *stimulins*. Later studies, especially those of Wright and Douglas, show that the substances in the serum, instead of stimulating the phagocytes, act upon the bacteria so as to fit them for engulfment by the phagocytes. These substances are the so-called **opsonins** and they appear to play an important part in natural resistance.

It seems probable that certain other substances **(lysins, antitoxins)** play some part in natural resistance. They seem to be of far greater importance, however, in acquired immunities (*vide infra*).

Natural immunity is rarely absolute, though we know certain examples; thus no animal, except man, has thus far been found susceptible to scarlet fever; and human beings are absolutely resistant to cattle plague. Natural resistance is, therefore, usually a relative matter, the resistance varying at different times and under different conditions of nutrition, work, climate, intoxication, mental anxiety, and the like. An important part of clinical medicine consists in finding out how natural resistance to disease can be increased by means of dietetic, hygienic, and other measures.

ii. Antitoxic Resistance

A natural resistance to intoxication also exists in addition to resistance to infection. This is well shown by comparing the amount of toxin necessary per kilogram of body weight to cause death in different animals. The amounts of tetanus toxin required for the horse, guinea-pig, rabbit, and chicken vary as the figures 1 :2 :2,000 :200,000. Measured in the same way, the mouse is 20,000 times less susceptible to the diphtheria toxin than the guinea-pig. It was believed by Ehrlich that natural resistance to toxic substances depends upon failure of the cells to anchor the poison chemically. Studies with Schick's reaction indicate that a large proportion of children and adults have enough antitoxin to diphtheria in their blood to protect them from infection. (See Diphtheria.)

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(c) *Acquired Immunity*

If a person has once had scarlet fever, smallpox, yellow fever, or measles, he is protected during the rest of his life from another attack. If he has had Asiatic cholera, he is protected for some time, but may, later in life, have a second attack. If he has had influenza, lobar pneumonia, or diphtheria, he may gain a protection for a very brief period, but in a short time is again susceptible, and, in some instances, more susceptible than if he had not been previously attacked. The degree and duration of acquired immunity are therefore variable for the different infections, and, in different people, for the same infection. A mild infection seems to yield as high a grade of immunity as a severe infection. Children who have a mild attack of scarlet fever, measles, or whooping-cough are therefore to be regarded as fortunate. Such observations of natural acquired immunity soon led to the attempt to immunize artificially with attenuated cultures of bacteria.

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i. Antibodies to the Antigens

Acquired immunity is partly due to an intensification of the natural powers of resistance, but it is principally due to the production of new protective substances by the organism and to changed conditions of the body **(allergy)**, which lead it, on threatened reinfection, to produce the protective substances in large amounts. These protective substances that the organism manufactures to overcome infection are known as **antibodies.** On the other hand, the substances of parasitic origin that excite the formation of these antibodies are known as **antigens.**

The antibodies formed include (1) substances that neutralize toxins (*antitoxins*), (2) substances that injure or destroy the bacteria (*bacteriolysins,* etc.), substances that act upon the bacteria, preparing them for phagococytosis (*immune opsonins or bacteriotropins*).

These substances are specific. The diphtheria antitoxin neutralizes the diphtheria toxin and no other; the agglutinins for the typhoid bacillus, agglutinate this and closely allied organisms and no others; the bacteriolysins produced in cholera infection, dissolve up the cholera vibrio and no other.

Though the earlier studies investigated only the antibodies formed against bacteria and toxins, later work has shown that cells of various sorts, especially red blood corpuscles, protein substances, ferments, etc., can act as antigens, and that they also give rise to specific antibodies (*cytolysins, hemolysins, precipitins, antiferments,* etc.).

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ii. Theories of Antibody Formation

Many theories have been advanced, but the **side-chain theory** of Ehrlich is the one that has dominated the thought of investigators, stimulating important research. This theory has never been completely substantiated, and though, at present, many of the foremost immunologists accept its tenets only in small part, and in many instances reject it in its entirety, it affords so ready a working hypothesis that it will be given here.

Ehrlich conceived of huge molecules in the protoplasm, each molecule having a more or less stable *central nucleus* to which are attached atomic groupings known as lateral chains, or *side-chains*, which, he believes, give the large molecule the power to enter into union with food substances and with other foreign substances reaching the cells. Accordingly, these side-chains have also been designated **receptors.** A foreign substance reaching a cell combines with its protoplasm only when it, in turn, possesses a suitable atomic grouping (**haptophore group**) for uniting with a receptor of the cell, much as a key fits into a lock, or as the fingers into a glove. Mere union of the foreign substance with the protoplasm of the cell does not imply that the former also exerts any influence upon the protoplasm other than mere occupation of the receptor. To influence the protoplasm, another special atomic grouping is required, a so-called *functional group;* in the case of a toxin the functional group is termed a **toxophore group.**

If a large number of receptors of a given kind in the cells become occupied by the haptophore groups of a given antigen, the cells begin to form receptors of the same sort in large amounts (Weigert's "law of regenerative over-compensation"), and the cells throw them off into the circulation as free antibodies, and these free antibodies can unite with the haptophore group of the foreign substance just as well as though they were attached to body-cells. Thus, for example, if the receptors of a cell have become sufficiently combined with diphtheria toxins in reaction duly formed receptors will be thrown off into the blood as diphtheria antitoxins. In other words, the same substance that, attached to the cell, is a prerequisite of its intoxication becomes a medium for cure when it is free in the circulating blood.

Examples of such free cellular receptors other than antitoxins are the antiferments, the agglutinins, the precipitins, and various amboceptors to be mentioned later.

On injecting antigens into an animal there may be a temporary depression of the mechanism of antibody formation (*negative phase* [1]); this is soon followed by an active production of antibodies (*positive phase*); later on, this over-activity returns to normal. As a rule, animals do not form antibodies against the substances of their own bodies, or of the bodies of animals of the same species.

Three kinds of receptors are distinguishable in the cell, designated by Ehrlich as receptors of the first order, of the second order, and of the third order.

Receptors of the first order possess only one haptophore group (e. g., antitoxins, antiferments). They have the power of anchoring only one foreign substance with the protoplasmic molecule. The *receptors of the second order* possess a haptophore group and a so-called ergophore, or zymophore, group (e. g., agglutinins and precipitins). With the haptophore group, the foreign substance is anchored to the protoplasm; through the ergophore group, the protoplasm is influenced.

The *receptors of the third order* possess two haptophore groups, one for anchoring a foreign substance (food molecules, bacteria), the other for anchoring complements from the blood serum through which the foreign substance is acted upon. This second haptophore group is called the complementophil group. A free receptor of this sort having two haptophore groups is known as an **amboceptor.**

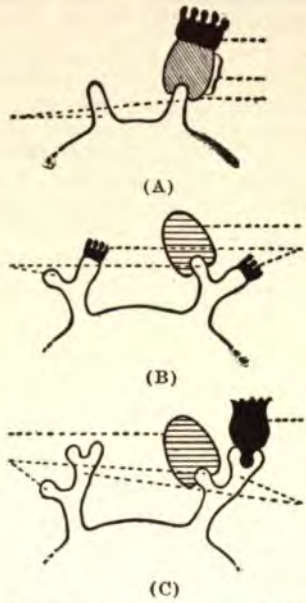

Fig. 40.—(A) Receptor of the First Order; (B) Receptor of the Second Order; (C) Receptor of the Third Order.

iii. Antitoxins

Powerful *antitoxins* can be produced in experimental animals against diphtheria toxin, tetanus toxin, snake venom, and the poisons of some of the higher plants. The sera containing the first two of these antitoxins can be carefully concentrated and injected into human beings for therapeutic purposes. The immunity thus produced is temporary and is known as a passive immunity, in contrast with the active immunity produced by the cells of the organism itself.

Antitoxins in an immune mother can pass through the placental circulation to the child. Antitoxins neutralize their corresponding toxins, but have no action upon the organisms that form the toxins. The chemical structure of antitoxins is unknown, but it is believed by some that they act by chemical union with the toxins to form a harmless substance.

A *toxin* has a haptophore group that unites with the cell and a toxophore group that exercises a deleterious effect upon the cell to which the toxin becomes attached. The antitoxins are free receptors of the first order and combine with the haptophore group of the toxin preventing union of the toxin with the sensitive cells.

[1] The existence of such a "negative phase" is denied by some investigators.

The toxophore group in the toxin is more sensitive than the haptophore group, and when injured by long keeping, or by heat, the toxin is transformed into an innocuous modification, the *toxoid.*

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iv. Bacteriolysins and Hemolysins

Serum containing *bacteriolysins* make the corresponding bacteria granular and dissolve them. Bacteriolysins have been especially studied in cholera, in typhoid, and in plague. In bacteriolysis, two distinct interacting substances are concerned. One is thermostable and specific—the **amboceptor or immune body**; the other is thermolabile and non-specific—the **complement**.

Amboceptors are non-dialysable, and may be kept for years. Complement is present in normal blood and degenerates rapidly *in vitro*. There are several varieties of complement, and their haptophore groups differ in their affinities. The complements possess, besides the haptophore group, functional or zymophore groups. The latter can be rendered inactive without injury to the haptophore group (formation of *complementoid*).

Hemolysins are similar in structure to bacteriolysins, and for hemolysis to occur three substances, (1) complement, (2) specific hemolytic amboceptor, and (3) red corpuscles must be present. When red corpuscles are mixed with a fresh serum containing specific hemolysins, the blood is laked, that is, the hemoglobin is dissolved out of the red corpuscles and diffused through the medium.

Normal serum has some hemolytic effect upon the red blood corpuscles of a different species (*natural hemolysis*), but these hemolytic properties of the serum of an animal can be greatly increased if the animal be subjected to repeated injections of washed corpuscles of a for-

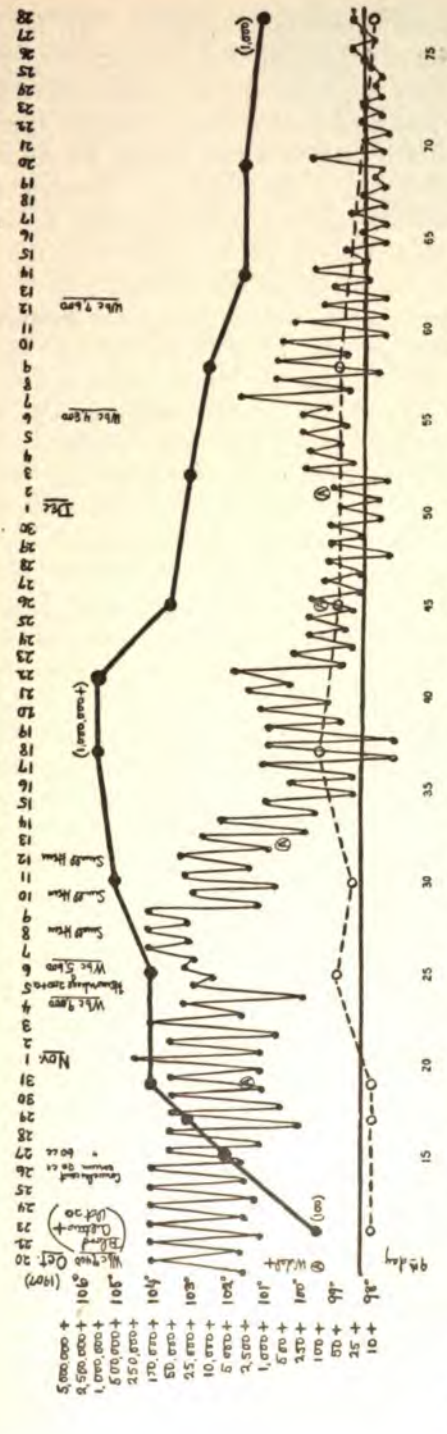

Fig. 41.—Diagram Illustrating How Bactericidal Power (B. P.) May Be Raised by the Addition of Complement In a Very Severe Case of Typhoid Fever. Heavy Black Line Represents B. P. with Addition of Complement; Dotted Line that Where No Complement was Added. (After H. S. Denison, J. H. H. Bull.)

eign species (*artificial hemolysis*). If, for example, a rabbit be subjected to a series of injections with sheep's red corpuscles, the serum of the rabbit will quickly hemolyse washed sheep corpuscles in a test tube. These artificially produced hemolysins are highly specific in their action.

Such a hemolytic serum heated for 30 minutes at 56° C. ceases to be hemolytic owing to destruction of complement, but when to such a serum, thus rendered inactive, a little normal serum (not hemolytic in itself) is added, its hemolytic power is restored, the reactivation being due to the addition of new complement to the thermostable amboceptor.

In terms of Ehrlich's theory, the **hemolytic amboceptor** possesses *two haptophore groups,* one with a strong avidity for red corpuscles (*cytophil group*), and a second for union (with less avidity) with complement (*complementophil group*). The cytophil group unites with red corpuscles, even at low temperatures. For union of the complementophil group with complement, a higher temperature is necessary. The amboceptor alone cannot hemolyze nor can complement alone; it is the complement that hemolyzes, by acting through the amboceptor; in other words, the function of the amboceptor is to act as a medium, connecting the complement with the red corpuscle. The complement itself here, as in the bacteriolysin, possesses not only the haptophore group for the union with the amboceptor, but also a zymotoxic, or ergophore, group that causes the laking. On heating to 60° C., the zymotroxic group of the complement is destroyed, but the haptophore group is uninjured, and can unite with the complementophil group of the amboceptor, the complement in this case having been changed to *complementoid*. There must be a certain amount of salt in the fluid in order that the complement may act. If the serum be freed from salt by dialysis, the complement is split into two parts, one part remmaining in solution, the other being precipitated. Complement itself must therefore have a very complicated structure.

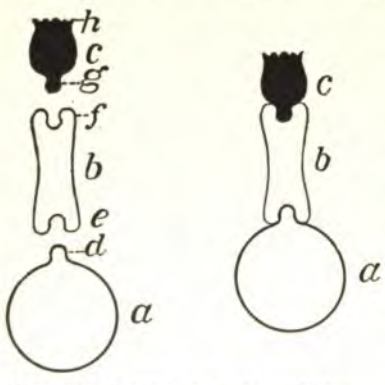

Fig. 42.—Schematic Representation of the Process of Hemolysis, (a) Blood Corpuscles, (b) Amboceptor, (c) Complement, (d) Receptor of the Blood Corpuscle, (e) Cytophil Group of the Amboceptor, (f) Complementophil Group of the Amboceptor, (g) Haptophore Group of the Complement, (h) Toxophore (Ergophore) Group of the Complement. (After Dieudonné.)

The researches of Preston Kyes indicate that in hemolytic snake venoms, lecithin can act as complement.

Recent studies indicate that extracts of certain organs exert a hemolytic effect (*organ hemolysis*), not unlike cobra venom hemolysis. This organ hemolysis appears to depend upon the lipoids in the extract. The theory has been advanced that some of the severe anemias depend upon

the hemolytic action of such organ lipoids, especially since ethereal extracts of the dibothriocephalus tape-worm act hemolytically.

According to Bordet, whose views are upheld in this country especially by F. P. Gay, the process of hemolysis is somewhat different from that assumed by Ehrlich. Instead of the term amboceptor, Bordet uses the term **substance sensibilatrice,** and instead of complement, the term **alexin.** According to Bordet, the red corpuscles are injured (sensibilized) by the substance sensibilatrice, after which the alexin causes laking.

The amboceptor has received various other names (e. g., *preparator* of Gruber; *fixateur* of Metchnikoff).

The hemolysins which act upon the red corpuscles of a different species are known as *heterolysins.* The blood of certain human beings contains hemolysins that act upon the red corpuscles of other human beings; that is, upon the cells of an animal of the same species. Such isolysins (or *isohemolysins*) may be of considerable importance when blood transfusion is contemplated for therapeutic purposes. W. L. Moss has worked out methods for securing human blood which will not act hemolytically on transfusion (see Diagnosis of Diseases of the Blood).

Hemolysins can themselves act as antigens, and, on injection, give rise to **antihemolysins,** which inhibit the hemolytic effect of a serum (production of anticomplement, or of anti-amboceptor, or of both).

Complement Deviation.—In studying bacteriolysis, or hemolysis, the quantitative relations of amboceptor and of complement must be considered. If, in test tube experiments, the amount of bacteriolytic amboceptor be greatly increased, while the complement remains unchanged in amount, there will be no bacteriolysis (*Neisser-Wechsberg phenomenon*). Here, probably, the combining power of the bacteria with amboceptors is more than satisfied, and free amboceptors remain in the surrounding fluid. If the complement be limited in amount, it will be distributed among the amboceptors attached to the bacteria and the free amboceptors; thus a part of the complement will be deflected (deviated) from the bacteria, and, with certain quantitative relations, the complement going to the attached amboceptors will be insufficient to cause bacteriolysis. It is possible that the attached amboceptors are less avid for complement than the free amboceptors.

Fixed Complement.—As described above, hemolysis depends upon (1) red blood corpuscles, (2) specific amboceptors (inactive immune serum), and (3) complement (fresh normal serum). Similarly, three constituents (bacteria, specific amboceptor, complement) are necessary for bacteriolysis. The complement can be the same in the two processes; the amboceptors are different. If one takes, for example, the serum of an animal immunized against the cholera vibrio, inactivates it by heat, adds cholera vibrios and complement and allows the mixture to stand for one hour at body temperature, the bacteriolytic amboceptors and the complement will

be anchored to the bacteria. If to this mixture we next add a hemolytic system consisting of red corpuscles anchored to hemolytic amboceptors without complement, no hemolysis will occur; the blood is not laked because the complement has been all used up; it has been "bound" or "fixed."

In another experiment, cholera vibrios are mixed with the inactive serum of an animal immunized against typhoid; complement is added, and the mixture kept for an hour in the thermostat at 37° C. Here specific bacteriolytic amboceptors for cholera vibrios are absent and the comple-

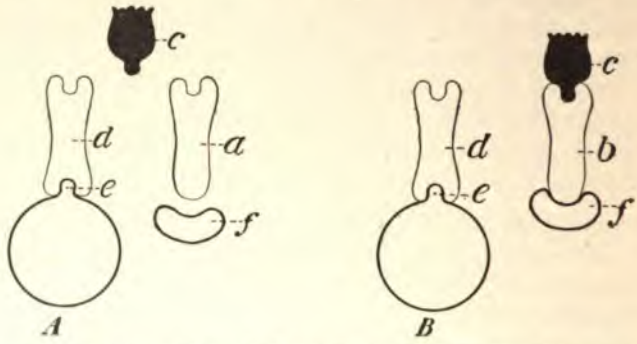

Fig. 43.—Schematic Representation of Complement Fixation and Hemolysis. (a and b) Immune Serum, (c) Receptor of the Blood Corpuscle—Hemolytic System, (d) Amboceptor—Hemolytic System, (e) Complement—Hemolytic System, (f) Antigen Bacillus, Blood Corpuscle. (After Dieudonné.)

ment will not be fixed. Now, if a hemolytic system be added (red corpuscles, plus specific hemolytic amboceptors), hemolysis will promptly occur, for the complement is free, and, uniting with the hemolytic amboceptors, will act through them upon the red corpuscles and will lake the blood.

Here we have a principle of great help in diagnosis, for, by testing for **complement fixation,** we can decide whether or not a serum contains specific amboceptors for a known bacterium. If the serum examined contain the specific amboceptor for the known antigen (Bacterium), there will be no hemolysis when the red corpuscles and hemolytic serum are added. If it do not contain these amboceptors, hemolysis will occur. The process of complement fixation is often called the **Bordet-Gengou phenomenon.** It is, clinically, especially important in the diagnosis of syphilis (Wassermann test, q. v.) and of helminthiasis, especially tenia and echinococcus.

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v. Opsonins

As has been stated, certain substances in the serum, which render bacteria susceptible to phagocytosis, are called opsonins (Wright and Douglas), or bacteriotropins (Neufeld). Those occurring in normal blood (*normal opsonins*) are probably entirely different from those occurring in the blood of immunized animals (*immune opsonins; bacteriotropins*). The immune opsonins are, according to Neufeld, thermolabile (consisting of complement and another body, the latter thermostable) and do not require complement for their activity. These substances have been studied in America especially by Hektoen, Ruediger, Cole, and Ross.

The methods of studying opsonins, we owe especially to Wright and Douglas. Clinically, Wright bases his method of treatment of infections with vaccines made from the infecting bacteria, upon a determination of the opsonic index (q. v.), which he uses as a guide for the injections.

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vi. Precipitins

These are antibodies that precipitate, specifically, protein substances from solution. The protein injected as an antigen is known as a *precipitinogen.* Through the immunizing process, *precipitins* are formed, which, when added again to a solution of the original protein (*precipitino-*

gen or *precipitable substance*) cause a precipitate to form. Ordinary protein precipitins are to be distinguished from bacterioprotein precipitins. The latter were discovered by R. Kraus in 1897, the former by Bordet and Tschistowitsch.

Ordinary Protein Precipitins.—The serum of an animal immunized against alien serum will cause precipitates in the alien serum when mixed with it. The principle is of great value in forensic medicine for differentiating the proteins of human, from those of animal, blood (Uhlenhuth). Nuttall has applied the principle most extensively in studying the biological relationships of animals.

Precipitins contain two groups, a more stable haptophore group, which unites with precipitinogen, and a more labile functional group, which causes the precipitation (Kraus and von Pirquet).

The biological test by means of precipitins is much more delicate than any known chemical test. Solutions of protein 1–100,000 are recognizable by the use of this method.

Bacterioprotein Precipitins.—Filtrates of old bacterial cultures yield precipitates with corresponding immune sera. The reaction is specific.

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vii. Agglutinins

These antibodies, discovered by Gruber and Durham, cause a clumping, or agglutination, of bacteria (*bacterio-agglutinins*) or of red blood corpuscles (*hemagglutinins*).

Normal serum contains agglutinins, which act upon the most different kinds of bacteria, if the serum be not markedly diluted (1:10 to 1:20). These agglutinins are not specific. The serum of a patient or of an animal immune to a given disease (like typhoid or cholera) from having had the disease naturally or from artificial immunization, agglutinates the corresponding bacterium in strong dilution (1:100 to 1:5,000, etc.). Such agglutinins are specific, and are therefore useful for diagnostic purposes (cf. Widal reaction). Bacteria, if motile, lose their motility when agglutinated, but are not necessarily killed; they will continue to grow, though often in the form of long interlaced threads (*thread reaction*).

Agglutinins are thermostable at 55° to 60° C., but are destroyed at 70° C.

Agglutinins contain two groups, (1) a *haptophore group,* which unites with the bacteria, and (2) a functional, or *agglutinophore, group,* which causes the agglutination. The latter is the more sensitive, and, when injured without injury to the haptophore group, the agglutinins are converted into *agglutinoids,* which can unite with bacteria without agglutinating them.

An immune serum may agglutinate other bacteria than the homologous bacterium, if they be closely related to it. Such **group agglutination** is met with especially in the typhoid-paratyphoid-colon group. In mixed infections, a serum may contain "immune" or "major" agglutinins for both infecting microbes **(mixed agglutination)**.

The **saturation experiment** of Castellani is used to distinguish between group agglutination and mixed agglutination. If the serum of a patient agglutinate typhoid bacteria in great dilution, and paratyphoid bacteria in almost as great dilution, a portion of serum is mixed with small amounts of a typhoid culture, allowed to stand for a time, and then centrifugalized. Should the serum subsequently continue to agglutinate paratyphoid bacilli, a mixed infection is assumed (mixed agglutination); otherwise a group agglutination is diagnosed.

Injection of red corpuscles of one species into an animal of another species causes hemagglutinins to appear in the serum; the immune serum will clump the red corpuscles of the animal-species the corpuscles of which have been used as antigen. Besides these hetero-agglutinins, hemagglutinins against blood corpuscles of an animal of the same species can be prepared (iso-agglutinins). As yet they have little, if any, diagnostic importance.

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viii. Antiferments

Similar to other antibodies are antiferments. They have been prepared against the lab-ferment, against trypsin, and against pepsin. (See Examination of the Blood.)

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(*d*) *Anaphylaxis; Hypersusceptibility; Allergy*

i. History and Definition

Studies on immunity have been directed chiefly to the explanation of the protection afforded by preceding infection. Since 1902, attention has been directed toward a contrasting group of phenomena described under different names—**anaphylaxis** (Richet), **hypersusceptibility** (Wolff-Eisner), or **allergy** (von Pir-

quet). The fundamental observations on which later knowledge of anaphylaxis is based were made by Héricourt and Richet (1898), when they noted that repeated injections of eel-serum into dogs causes increased susceptibility to that substance. Later, Richet (1902) found that if a dog be injected with a poison derived from the sea-urchin, and several days later be given a second injection, the second dose need be only $\frac{1}{4}$ or $\frac{1}{5}$ as large as the first dose to produce severe or lethal symptoms. If the animal lives, he recovers more quickly than after the first injection. Richet therefore assumed that the poison consists partly of an immunizing or prophylactic principle and partly of a sensitizing or anaphylactic principle. This was the first sharp separation of the conception of **anaphylaxis** from that of immunity. Soon after the appearance of Richet's publications, Arthus confirmed his observations. Arthus noted that rabbits injected with horse serum become exquisitely sensitive to a second injection given after an interval of 7 days.

A little later, von Pirquet observed that, on giving a second injection of horse serum to a child, the symptoms of serum disease did not appear on the 10th day, as after the first injection, but within 24 hours, from which he drew the conclusion that, in infections, the disease-exciting agent gives rise to pathological symptoms only after it is altered by antibodies, and that the **incubation period** is the time elapsing before the formation of antibodies. Later, in collaboration with Schick, the difference between *accelerated* and *immediate* capacity for reaction was recognized by von Pirquet and the diagnostic significance of the latter pointed out. These authors came to the conclusion that the antibodies produced convert the foreign body injected (innocuous in itself) into a toxic modification.

In 1902, Theobald Smith had noticed that guinea-pigs used for testing diphtheria toxin, and for that purpose injected with toxin-antitoxin mixtures, often died if, after a short interval, they were given a small amount of horse serum by subcutaneous injection. Otto confirmed and elaborated these findings.

Rosenau and Anderson, in an attempt to explain sudden deaths after treatment by diphtheria antitoxin, made an exact study of the effect of horse serum, and of other substances, upon guinea-pigs.

In 1904, the subject was taken up by Wolff-Eisner, who introduced the term **hypersusceptibility,** and suggested that hay fever and urticaria are to be explained on this principle.

In 1906, von Pirquet suggested the expression **allergy,** or clinical alteration of reaction capacity, as a name for the phenomena formerly included under the terms anaphylaxis and hypersusceptibility. In America, important contributions to the subject have been made by Auer and Lewis, Gay and Southard, Adler, Pearce, Helmholz, P. W. Clough, Lucas, E. L. Trudeau, V. C. Vaughan, H. G. Wells, H. Zinsser and C. R. Austrian, besides those already mentioned.

In studies of *vaccination and re-vaccination,* it has been shown that the change in the reaction capacity of the body (allergy) is easily elicited by successive vaccinations of the skin with cow-pox. The reaction capacity is changed as regards its time-relations, both qualitatively and quantitatively. On a first vaccination, the inflammation reaches its maximum about the 11th day. On repeated vaccinations, it may appear on the 9th to the 4th day after the vaccination (*accelerated reaction*).

In the allergy following *injection of foreign serum,* similar temporal changes in reaction capacity are met with. The normal "serum disease" appears about the 9th day. If more serum of the same sort be injected after an interval of several months or years, the symptoms of serum disease appear in from 4 to 7 days (*accelerated reaction*). If the second injection be made intravenously at a certain interval after the first, symptoms appear very quickly (*immediate reaction*).

Besides these temporal changes in reaction capacity, quantitative and qualitative changes are demonstrable.

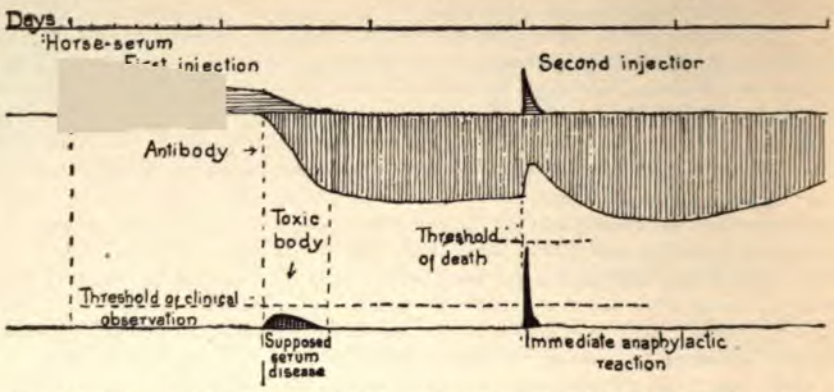

Fig. 44.—Effects of Horse-serum in Man. (After C. E. von Pirquet, Arch. Int. Med.)

Any soluble foreign protein (of animal, of vegetable, or of chemical source) may act as a sensitizing substance if it reach the blood or lymph in its native or unaltered state, uncleft. Exceedingly minute quantities suffice to induce sensitization. H. G. Wells showed that 0.000.000.05 g. of crystallized egg albumen can make a guinea-pig sensitive. Ordinarily, 0.1 to 1.0 c.c. of a foreign serum will so sensitize a guinea-pig that a second injection given intravenously will cause anaphylactic death.

Sensitization may occur in ways other than by injection. It may be *inherited*. It may sometimes be established by *feeding* a foreign protein. It may occur after

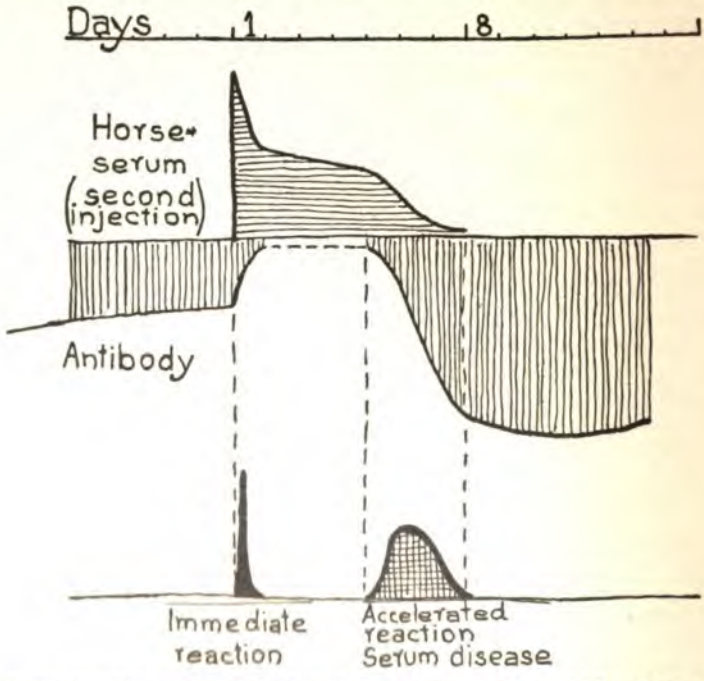

Fig. 45.—Double Reaction after Reinjection of Horse-serum in Man. (After C. E. von Pirquet, Arch. Int. Med.)

instillation of serum into the conjunctiva, or after *inhalation* of serum. Guinea-pigs can be sensitized by *inunction* of horse-serum-lanolin salve (Clough), or by *vaginal irrigation*, or *rectal enema*. We begin, through such studies, to understand the origin of the so-called *idiosyncrasies* of man. It is to be kept in mind that these sensitizations are very specific; thus the *organ-proteins* of an animal are different from the *serum-proteins* of the same animal.

The blood of an animal which has been sensitized to a protein substance **(active anaphylaxis)** may, when injected into another animal, lead to a transference of the allergy to the second animal (*passive allergy;* **passive anaphylaxis**). Anaphylaxis can also be passively transferred from mother to young.

Under certain circumstances an allergic condition can be suppressed (*anergy;* **antianaphylaxis**).

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*Doerr (R.). Allergie und Anaphylaxie. In: Handb. d. pathogen. Mikroörg. (Kolle & Wassermann). 2. Aufl. Jena, **1913**, ii, 2, 947–1154.*

ii. Characters of Allergy, and Symptoms of Anaphylactic Reaction

The three main characteristics of the allergic change are (1) shortened incubation period, (2) accelerated course of the phenomena of reaction, and (3) accentuation of the symptoms of reaction. In the typical acute anaphylactic shock, such as follows injection of serum into a sensitized guinea-pig, there is restlessness, cough, sudden severe dyspnea, soon followed by clonic spasms, and by death within a few minutes. In milder shock, the dyspnea is transitory, the animal recovers quickly, and, in a few hours, may seem normal again. When such an animal recovers after re-injection, it is immune for a short time to subsequent injections of the same serum (anergy; anti-anaphylaxis).

It has also been shown that death from anaphylactic shock is ac-

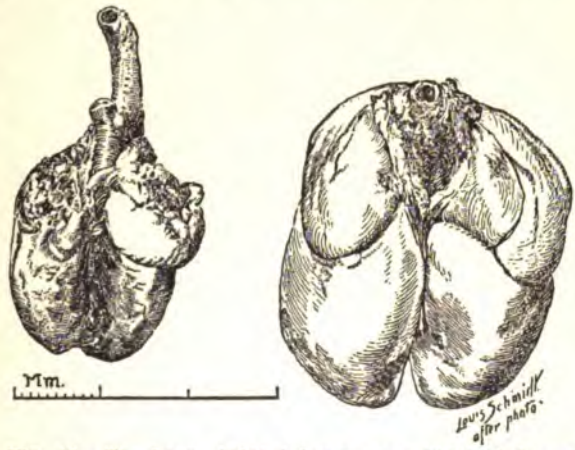

Fig. 46.—The Large Inflated Lungs were Obtained from a Typical Fatal Case of Horse-Serum Anaphylaxis in a Guinea-pig. The Small Collapsed Lungs Belonged to an Anaphylactic Guinea-pig of the Same Lot which was Saved by the Injection of Atropin. This Animal Seemed Normal when Killed. The Picture Shows Strikingly the Characteristic Lung Picture of Anaphylaxis and the Remedial Effects of Atropin. The Right Vagus had been Resected in Each Guinea-pig Thirteen Days Before the Toxic Injection. (After J. Auer.)

companied by fall in blood pressure (dog), emphysema of the lungs from bronchospasm (Auer and Lewis), fall of temperature (guinea-pig), and "chemical rigor" of the myocardium (rabbit). Common to allergy in all these varieties are (1) leukopenia, (2) loss of the coagulability of the blood, and (3) disappearance of complement from the blood.

Phenomena of Serum Disease.—The symptoms that follow a single injection of horse serum, the so-called **serum disease** (von Pirquet and Schick), appear, after an incubation period of 8 to 12 days, in the form of (1) urticaria, usually starting at the site of injection and extending to other parts of the body, (2) edema, (3) arthralgias, (4) swelling of the lymph glands, and (5) fever, with albumin and casts in the urine. The larger the dose of serum, the more marked the symptoms in predisposed persons.

On re-injection of a serum derived from the same animal species, the symptoms of serum disease appear more quickly (4 to 7 days). If the second injection be made in 3 to 8 weeks after the first, over 90 per cent of those injected will show signs of serum disease. On re-injection after 6 to 9 months, about 50 per cent of the cases show symptoms. Sometimes a single cubic centimeter, on re-injection, will suffice to cause symptoms.

Care should always be exercised in giving diphtheria antitoxin, inquiry being made regarding a previous injection. Antitoxins made from animals other than the horse should be made available, and used for second injections given after intervals longer than a week.

Clinical Conditions Due to Anaphylaxis.—High fever and urticaria appear to depend upon anaphylactic reaction to foreign proteins. The study of bronchial asthma, and of hay fever, bids fair to be revolutionized by the study of sensitizing "asthmogenic" substances. The tuberculin reactions of various sorts are believed to be anaphylactic phenomena. Indeed, it would appear that the symptomatology of all the infectious diseases must sooner or later be re-written in terms of allergic reaction, and a start in this direction has already been made.

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iii. Antianaphylaxis

Methods of desensitizing sensitized persons, that is, the production of so-called *anti-anaphylaxis,* or *anergy,* should be more carefully studied. In

animals, desensitization can be produced by the intravenous injection of a minute quantity of the antigen, or of a series of graded doses thereof (Besredka). In animals, a whole series of substances may on injection prevent the anaphylactic reaction; among these may be mentioned NaCl, $BaCl_2$, peptone, ether, atropin; urethan, adrenalin, and chloral hydrate.

In man, severe serum anaphylaxis is not very common, especially since we have learned to take certain precautions (use of *old* serum; use of *purified* serum; avoidance of repetition of horse serum injections; caution in patients who suffer from asthma or who have asthmatic antecedents). In patients who have had antitoxin before, I have sometimes given a small amount of serum by the rectum on the day preceding re-injection of diphtheria antitoxin. If we fear anaphylaxis, it is well to use the **desensitizing methods of Besredka,** to be on the safe side. In urgent cases, e. g.,

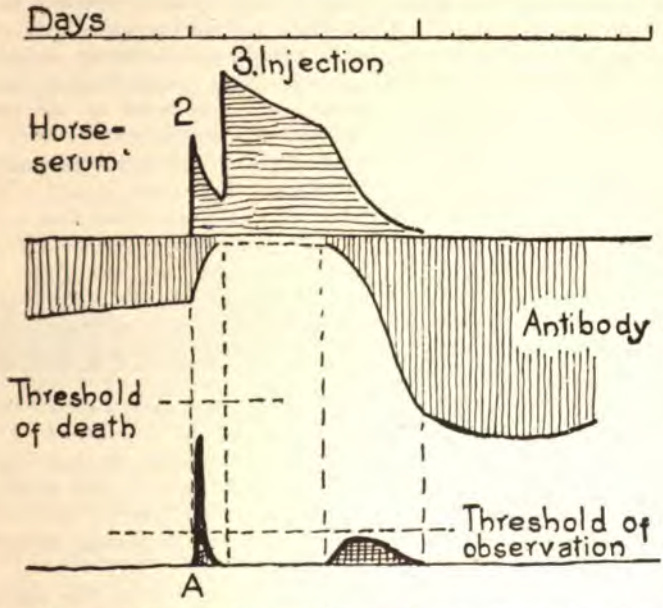

Fig. 47.—Anergy—Anti-anaphylaxis. (After C. E. von Pirquet, Arch. Int. Med.)

of cerebrospinal meningitis, Besredka advises 1 c.c. of a 10 per cent solution of serum intravenously; after 4 minutes, 3 c.c. more; and 10 minutes later 10 c.c.; after 2 more minutes 25 c.c. of the dilution. Four minutes after this last dose, the patient is desensitized and may receive 10–30 c.c. of undiluted serum, either intravenously or intraspinally.

The danger seems to be greatest in patients who suffer from vasomotor instability, or from vagotony. The fatal cases in human beings have most often been asthmatics, or persons with asthmatic antecedents.

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iv. Theories of Allergy

It seems certain that the active agent in anaphylaxis circulates in the blood (passive transference!), though it doubtless is derived from the body cells. Some think that this is a single substance (*anaphylactin*). Others believe that the "anaphylactins" vary in the different allergic states. Von Pirquet calls the substance *ergin*, and believes it to be an antibody, produced by the antigen, and capable of converting the latter into a poisonous substance.

On account of the resemblance of anaphylactic shock to the **anaphylactoid phenomena** (Auer), which appear in poisoning by a first injection of peptone, or of certain other substances, the theory has been advanced that some *protein cleavage* ("parenteral digestion theory" of anaphylaxis) must occur during the anaphylactic reaction, and this view receives much support from experiment (Vaughan; Schittenhelm and Weichardt; Biedl and Kraus). The view generally held at present is that a first parenteral introduction of protein into the body causes sensitization by the production of antibodies (proteolytic ferment?) which, on subsequent injections, unite with the antigen to lead, in some way, to intoxication by a protein cleavage-product that excites the symptoms of anaphylaxis (Vaughan). Vaughan has shown that any protein can be split into a *toxic fraction* (alcohol-soluble) and a *non-toxic fraction*, and that, on first injection into a guinea-pig, the toxic fraction will cause symptoms and anatomical signs like those of anaphylactic shock. Strange to say, the toxic fraction does not sensitize, but the non-toxic fraction can sensitize against the whole protein molecule, though not against itself.

In general anaphylaxis, the poison appears to act upon the central nervous system, especially upon the vasomotor center; this action can be inhibited by narcosis with ether, ethyl chlorid, and urethane (Besredka).

By far the best reviews in English of the present state of our knowledge regarding anaphylaxis are to be found in Auer's article "The Functional Analysis of Anaphylaxis," in Forchheimer's "Therapeusis of Internal Diseases," 1914, V, 39-120, in Zinsser's article in his "Infection and Resistance" and in von Pirquet's articles on "Allergy."

B. The Body Temperature

Measurements of the body temperature form an important part of every clinical study.

1. Heat Regulation

In warm-blooded animals (*homoiothermic*), a tolerably constant temperature is maintained within the body, despite the temperature of its surroundings; in the cold-blooded animals (*poikilothermic*), the temperature of the body changes with that of its surroundings. In man, the temperature normally remains fairly constant, varying not more than 1° to 1.5° F. in the 24 hours.

Animal heat arises from the combustion going on in the body (oxidation of proteins, fats and carbohydrates by the inhaled oxygen). A human being of average weight and at rest uses up in twenty-four hours about 2400 calories; of these about 80 per cent are given off in radiation, conduction and evaporation of water from the skin, about 12 per cent by evaporation from the lungs, while about 8 per cent are used up in warming the food intake and the inspired air. Oxidative processes in all the organs give rise to heat, but the largest amounts of heat are produced in the muscles, and in the glandular tissues generally, especially in

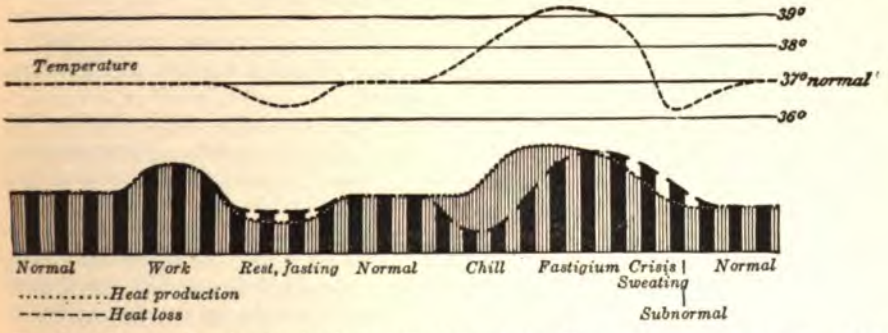

Fig. 48.—Diagram Showing Mechanism of Heat Regulation Under Different Conditions. (After H. H. Meyer and R. Gottlieb, "Pharmacology, Clinical and Experimental," published by J. B. Lippincott Co., Phila.)

the liver. The *self-regulatory mechanisms* are partly physical, partly chemical, in nature. In man, physical regulation predominates. Among the *physical methods of regulation* are included:

(1) Artificial regulation, by means of clothing and housing.

(2) Natural regulation. (a) Through circulatory changes (anemia or hyperemia of the skin). (b) Evaporation of water from the skin and lungs. The *chemical regulation* occurs through increase or decrease of the oxidative processes going on in the body. These have to do with heat production in contrast with the physical regulation, which has to do with heat dissipation. Many factors influence heat production; among the more important are (1) bodily exercise, (2) food intake, (3) influences acting upon catabolism, especially certain internal secretions (*e. g.*, thyroid) and ferments, especially the oxidases.

The automatic self-regulation is often disturbed in disease so that the organism is no longer able to maintain the normal temperature. Owing

to a disproportion between heat formation and heat dissipation the tem perature may become higher than normal (*fever,* or *pyrexia*), or lowe than normal (*subnormal temperature*).

Fever is usually due to increased heat production rather than t lessened heat loss, especially in the infectious diseases. During a chill there is rapid increase in temperature owing to the muscular contraction during the rigor. Heat loss is somewhat diminished as a rule while th temperature is rising, though when the temperature reaches higher level the loss of heat is usually increased. During the sweat following a chill heat dissipation may be greatly increased (from cutaneous hyperemia and evaporation of water). Every gram of water evaporated from the skin withdraws from the body about 0.6 calories or about 1/7 of the heat tha arises from the combustion of 1 gram of protein, or of carbohydrate, in th body. A loss of 4 liters of sweat could withdraw 2400 calories, or a amount equal to the daily loss of an individual at rest.

In heat regulation, a number of centrifugal nerves, going to the muscles, bloo vessels, sweat glands and respiratory organs are concerned. These nerves appe to stand under the dominion of a *nerve center for heat regulation.* The location this center has not been definitely determined. Puncture of the corpus striatu causes increase of temperature through increased heat production, owing chiefly t increased carbohydrate combustion (O. Scholtze). Fasting animals, and glycogen free animals, react very little to such a puncture.

It seems probable that the mechanism of heat regulation is acted upon by sub stances like peptones, bacterial proteins, toxins, and certain salts. Large amounts of these substances cause a rapid fall in temperature, smaller ones a rise in temperature. Substances that increase temperature are said to be *pyrogenic.*

Increased loss of heat may be due to reflex influences that act by increasing the respiration or through the vasodilators; and, again, reflex influences may cause fever through vasoconstriction, though the fevers usually designated as reflex (gall-stone fever; urethral fever) are probably not reflex, but due to the setting free of pyrogenic substances in local infectious processes.

2. Measurement of the Body Temperature (Thermometry)

For this purpose a clinical thermometer, exactly tested, is used. In this country, and in England, the Fahrenheit scale is employed, while on the Continent, the Centigrade scale is in use. Quick-registering, maximal thermometers are now universally employed.

The temperature may be taken by *mouth* (under the tongue), in the *axilla,* or by *rectum.* In this last, the temperature is 0.5° to 1° C higher. For exact measurement, rectal temperatures are the more satis factory, and they should always be used for taking the temperature in children, in very old people, or in adults with disturbed mentality.

In ordinary clinical work the temperature is taken at least twice a day but, when the temperature is varying much, it may be desirable to measur

it more frequently (every 2, 4, or 6 hours). The results are recorded on a **temperature chart,** in the form of a continuous curve. Such continuous curves, with accompanying pulse curves and respiration curves, as charted by a trained nurse, are very helpful for quick orientation in clinical studies.

For converting the scale of one thermometer into that of another, the following formulæ are used:

F = Fahrenheit.
C = Centigrade.
R = Reaumur.

To convert	Fahrenheit to Centigrade	$\frac{5\ (F-32)}{9}=C$
To "	Centigrade to Fahrenheit	$\frac{9}{5}\ C+32\ =F$
To "	Fahrenheit to Reaumur	$\frac{4\ (F-32)}{9}=R$
To "	Reaumur to Fahrenheit	$\frac{9R}{4}+32=F$

Thus

96° F. = 35.5° C.	99° F. = 37.2° C.	103° F. = 39.5° C.
97° F. = 36.1° C.	100° F. = 37.8° C.	104° F. = 40° C.
98° F. = 36.6° C.	101° F. = 38.3° C.	105° F. = 40.5° C.
98.6° F. = 37° C.	102° F. = 38.9° C.	106° F. = 41.1° C.

For the conversion of degrees Fahrenheit to degrees Centigrade, I have found the following diagonal line on millimeter paper very convenient. The ordinates represent °C., the abscissæ °F. I am indebted to our physicist, Professor Joseph S. Ames, for calling my attention to this simple plan. (See next page.)

Reference

Bolton (*H. C.*). *Evolution of the thermometer, 1592–1743.* 12°. *Easton, Pa.,* ***1900.***

3. Normal Temperature of the Human Body

The normal rectal temperature of the human body varies between 98.5°–98.9° F., the axillary temperature between 97.6°–98.3° F. Plethoric individuals show a little higher temperature; delicate, anemic individuals a little lower.

During the 24 hours the normal temperature varies slightly, in the form of a curve which is higher in the evening than in the morning, after eating than when fasting, and after exercise than when resting; the temperature rises also after a hot bath. The minimal temperature of the 24

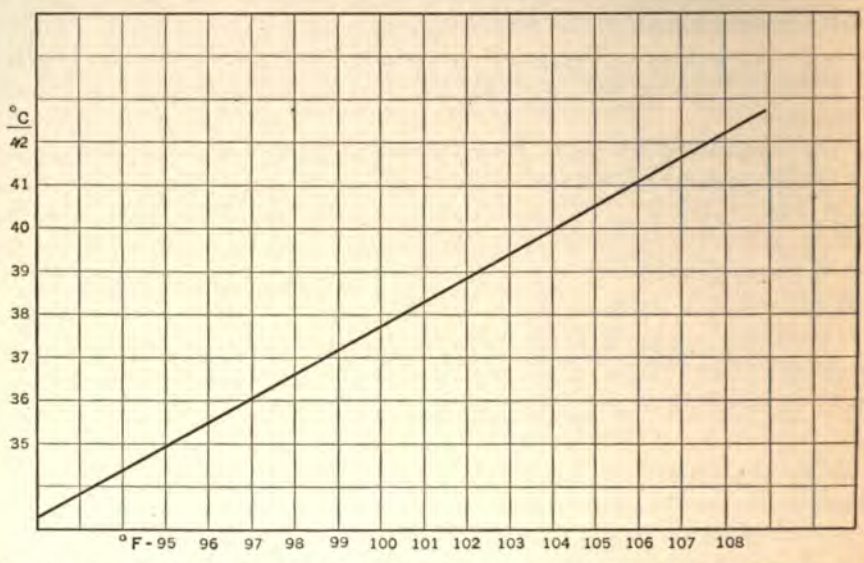

Fig. 49.—Easy Method of Translating Degrees Centigrade into Degrees Fahrenheit and vice versa. Note that the Vertical Lines Correspond to Degrees Fahrenheit, and the Horizontal Lines to Degrees Centigrade where the mm. Chart is Cut by the Black Oblique Line. (Courtesy of Prof. J. S. Ames.)

hours is observed between 2 A. M. and 6 A. M., the maximal temperature between 5 P. M. and 8 P. M. When patients lie in bed the whole 24 hours, the daily variations are much less than when they are up and about.

The temperature of sucklings and of young children is normally a little higher than that of adults.

4. Fever

Fever is the name given to pathological elevations of the body temperature.

(*a*) *Febrile Temperatures*

The following fever scale shows, at a glance, the terms ordinarily in use to designate the different deviations from normal temperature:

Name.	*Fahrenheit.*	*Centigrade.*
Subnormal temperature (collapse)	Below 96.8°	Below 36.0°
Subfebrile temperature	" 99.5°–100.4°	" 37.5°–38°
Slight fever	" 100.4°–101.2°	" 38° –38.4°
Moderate fever	" 101.2°–103.2°	" 38.4°–39.5°
Rather high fever	" 103.2°–105°	" 39.5°–40.5°
Very high fever	Above 105°	Above 40.5°
Hyperpyrexia	" 107°	" 41.6°

In rare cases, temperatures have been recorded as high as 113° F., or even as high as 122° F. (English Commission).

The lowest temperatures observed in human beings have been in cases of brain tumor, especially of tumors of the fourth ventricle, 73.4° F. (Lemcke), 86°–89.6° F. (Reinhold).

The daily variations in the temperature curve are more outspoken in febrile patients than in healthy individuals. The temperature often falls markedly in the early morning hours (*morning remission*), to rise considerably in the later part of the day (*evening exacerbation*). Occasionally, an opposite behavior is met with, the temperature being higher in the morning than in the evening (*inverted type*).

With the sudden onset of high temperature in infectious disease, the patients often suffer from chilly sensations, or have an outspoken **rigor** or **chill.** This is especially often met with in malaria, in sepsis, in endocarditis, and in the beginning of lobar pneumonia. The patients complain bitterly of cold, their teeth chatter, and the whole body may shake. The skin is pale and cool (vasoconstriction). After the chill, there may be marked cutaneous hyperemia with sweating, especially if the temperature fall rapidly.

(*b*) *Different Types of Fever*

An analysis of various fever curves permits of a subdivision into several types, according to the variations shown. The more important of these are the following:

i. Continued Fever (Febris continua)

Here the curve is fairly level, the daily variations being slight, not greater than 1° C. Such a continued fever is seen especially in the second stage of typhoid fever, in most of the acute exanthemata, in croupous pneumonia, in tuberculosis, etc.

ii. Remittent Fever (Febris remittens)

Here there are marked daily variations, greater than 1° C., a fall in temperature occurring usually in the morning hours, though even then the temperature does not reach normal. Such a remittent fever is seen in the third stage of typhoid fever (amphibolous period), in acute articular rheumatism, in various septic diseases, in pulmonary tuberculosis (hectic fever with night sweats).

iii. Intermittent Fever (Febris intermittens)

Here the minimal temperature in the 24 hours may be normal or subnormal, while the maximal temperature may be very high. Brief periods

of fever (*febrile paroxysms*) alternate with brief afebrile intervals (*apyrexia*). Such an intermittent fever is met with especially in malaria of different types (quotidian, tertian, quartan), in sepsis, in miliary tuberculosis, etc.

iv. Recurrent Fever (Febris recurrens)

Here several days of fever are followed by several days of apyrexia. Such a recurring fever is characteristic of the relapsing fever due to the *Spirochaeta obermeieri*. It is sometimes met with in Malta fever, and in some cases of Hodgkin's disease (recurring fever of Pel).

(c) *Stages of the Febrile Course*

A single fever curve is divisible into three parts:

1. Stage of rising temperature **(stadium incrementi)**, with or without chill.
2. The height of the fever **(fastigium** or **acme)**.
3. Stage of falling temperature **(stadium decrementi** or **defervescence)**. The temperature may fall suddenly **(crisis)**, often accompanied by sweating, as in lobar pneumonia; or slowly **(lysis)**, the temperature becoming markedly remittent or intermittent and taking several days to become normal, as at the end of typhoid fever.

When the temperature falls quickly, but is followed by a slight singe elevation, we speak of a *protracted crisis*. When the temperature rises unusually high, just before the crisis, we speak of a *"critical perturbation"*. In typhoid fever, between the fastigium and the stadium decrementi, there is often a period of markedly remittent temperature known as the period of *steep curves*, or so-called *amphibolous stage*.

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C. Clinical Applications of Bacteriological Methods

For purposes of clinical diagnosis in the infectious diseases, an acquaintance with bacteriological methods is essential. Every medical student is nowadays trained in the study and isolation of the pathogenic forms of bacteria. The methods of bacteriology are fully described in the special text-books on the subject. Here only a few of the methods particularly applicable in clinical work are given. For other methods the student may consult the treatises of V. A. Moore, Hiss and Zinsser, E. O. Jordan, Kolle and Wassermann, Kraus and Levaditi, Brugsch and Schittenhelm, Park and Williams, E. R. Stitt, and others.

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1. Collection of Material for Bacteriological Examination

Great care must be taken in collecting material to avoid contamination with extraneous bacteria.

Secretions.—Secretions from the oral, nasal and pharyngeal cavities and from the urethra, vagina or cervix are best collected by means of a sterile platinum loop.

If possible, smears and cultures should be made immediately, as the materials often dry in transport, in which case certain microörganisms (e.g., gonococci, meningococci) die out. When the physician cannot make the examinations himself, he may secure the material by means of a sterile swab, and inclose it in a sterile test tube, such as is now provided by the Health Department of every town.

Sputum.—This, as ordinarily collected, is worthless for bacteriological examination. According to Luetscher, sputum is best collected by placing a sterile Petri dish beside the patient and explaining to him that what is wanted is not saliva nor ordinary pharyngeal hawkings, but the sputum which can be felt to come from the bronchi. It is best to secure that coughed up in the morning from the depth of the bronchi. It is desirable that this should be worked up as quickly as possible. If sputum, so collected, be washed thoroughly by the bacteriologist in several Petri dishes of sterile salt solution, the pathogenic agents can usually be obtained, in almost pure culture, from the interior of the washed mass.

Feces should be collected directly, in a large sterile glass vessel. For amebæ, the mucus obtained in the eye of a rectal tube may be examined.

Urine.—This should be drawn by sterile catheter after thorough cleansing of the meatus and glans. The centrifugate may be examined microscopically, by cultural methods, or by animal inoculation.

Exudates, Transudates, Pus and Cerebrospinal Fluid.—These are best collected with the aid of a sterile aspirating syringe.

Blood.—If only small amounts are required (search for malarial parasites, Widal test, opsonic index, etc.), the blood can be obtained from the lobule of the ear, or the tip of the finger, after carefully cleansing with alcohol and ether and drying. (See Examination of Blood.) If larger amounts are needed (blood culture; Wassermann test; other complement fixation tests), 20-100 c.c. of blood can easily be withdrawn from a vein at the bend of the elbow by means of a suitable syringe (Luers; Record). A ligature is placed around the upper arm and made tight enough to obstruct the venous flow without obliterating the radial pulse. Aseptic precautions!

C. E. Simon's Method.—When it is not feasible to secure blood as above, a sufficient quantity of blood for the Wassermann test (0.5-1.5 c.c.) can be secured by freely puncturing the lobule of the ear at its margin and then "milking" the ear into a little glass tube, measuring about 5 cm. in length with a diameter of 5-6 mm., the individual drops being scooped up with the edge of the tube.

K. D. Blackfan's Apparatus for Collecting Infants' Blood for the Wassermann Reaction.—The methods usually employed for obtaining blood from infants are in the majority of instances extremely unsatisfactory. The veins are too small to enter and it is a tedious, difficult and painful procedure to collect the necessary amount of blood by puncturing the fingers or toes.

The apparatus herein described is a simple, inexpensive device by which the necessary amount of blood can be obtained easily, with a minimum of discomfort to the patient and in a comparatively short space of time. The time spent in collecting the blood averages about 2 minutes.

The apparatus, as shown in Fig. 50, consists of a glass cylinder (A) 1⅝ inches in diameter; the large end is ground smooth and the other end (B) is drawn out for the attachment of a small hand suction pump (C); an outlet (D), which is fused at an angle to the under surface of the cylinder, ½ inch from the large end, and a collecting tube (E). The collecting tube (E) fits over the outlet (D), the connection being made air-tight by means of a small piece of rubber tubing. The tube in which the blood is collected may be the size which is used in the laboratory test, obviating the necessity of transferring the blood to another tube.

Technic with Blackfan's Apparatus.—The technic is as follows: Connect the

apparatus for use. The patient may be placed in either the upright or recumbent posture. The most convenient site is on the back just below the angle of the scapula, though any other surface of the body may be used. Having cleansed the area with alcohol and ether, one or two small punctures are made through the skin with a sharp-pointed scalpel or Hagedorn needle and the apparatus is quickly applied. With but little suction-force the blood will flow from the wound through the outlet and into the collecting tube. After a sufficient amount has been collected, the tube is taken off, a cotton plug is inserted and the tube containing the blood is set aside until the examination is made. The wound is covered with a collodion dressing and the resulting swelling rapidly subsides with no discomfort to the patient.

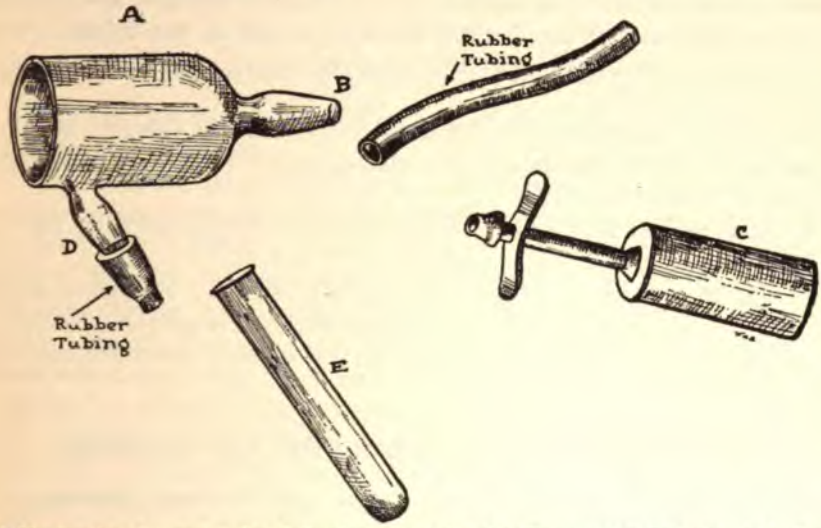

Fig. 50.—Suction Apparatus for Collecting Blood for the Wassermann Reaction, (A) Suction Glass Connecting at (B) with Suction Pump (C); the Blood Flows Through (D) Connected by Rubber Stopper with an Ordinary Test Tube (E). (After K. D. Blackfan.)

Blood may be collected by this method from the older children and adults, as well as infants, in a much shorter time and with less difficulty than by entering a vein.

The glass apparatus can be made in the laboratory or by a glass blower and the suction pump can be obtained through any surgical supply house.

With sufficient care, blood so obtained may be used also for blood-cultures from infants' blood, though there will often be contaminations by skin cocci.

Of course, blood obtained in this way should never be used for a blood count, hemoglobin estimations or for physical and chemical determinations, as the result would be of no value. For serological tests, however, this method is very valuable.

2. Kinds of Bacteria Often Found

In Nasal Secretion.—Staphylococci; diphtheria bacilli; lepra bacilli; meningococci; encapsulated bacilli in ozena and in rhinoscleroma.

In Conjunctival Secretion.—Gonococci; influenza bacilli; diphtheria bacilli; xerosis bacilli; pneumococci (serpiginous ulcer).

In Pus.—Pyogenic cocci; colon bacilli; bacillus pyocyaneus; tubercle bacilli.

In Pharyngeal Exudate.—Diphtheria bacilli; streptococci; fusiform bacilli; a spirillum (Plaut-Vincent's angina); meningococci; pneumococci; influenza bacilli.

In Sputum.—Tubercle bacilli; pneumococci; influenza bacilli; streptococci; staphylococci; actinomyces; glanders bacilli; anthrax bacilli; plague bacilli.

In Feces.—B. typhosus; B. paratyphosus; B. dysenteriæ; B. coli; cholera vibrios; dysenteric amebæ; tubercle bacilli, etc.

In Urethral and Other Genital Secretions, and in the Urine.—Gonococci; tubercle bacilli; typhoid bacilli; streptococci; staphylococci; colon bacilli; smegma bacilli.

In Pleural Tappings.—Pneumococci; streptococci; tubercle bacilli.

In Peritoneal Tappings.—Colon bacilli; typhoid bacilli; streptococci; gonococci; tubercle bacilli.

In Cerebrospinal Fluid.—Meningococci; tubercle bacilli; pneumococci; influenza bacilli; trypanosomes.

In Blood.—Typhoid bacilli; paratyphoid bacilli; streptococcus viridans; streptococcus hemolyticus; other streptococci; staphylococcus; pneumococcus; anthrax bacilli; plague bacilli; bacilli typhi-exanthematici, etc.

3. Microscopic Examinations for Bacteria

(*a*) *Examination of Dried, Fixed, and Stained Smears*

This is the most useful method for quick clinical orientation.

The Smear.—A minute amount of the material is evenly *spread* on a clean cover glass or slide, in a very thin layer, by means of a platinum loop or the end of a clean match.

Air-Drying.—The preparation is allowed to *dry* completely in the air; the process may be hastened by holding the smear, with the film side up, a few inches from a very low gas flame, avoiding, however, any temperature that could coagulate protein, since the fixation should not be made until the air-drying is complete.

Fixing.—For *fixing*, the smear is passed three times directly through the flame, with the film side up. This coagulates the protein, making it insoluble. Care must be taken to avoid over-heating. A still better fixation, desirable when one wishes to study the finer details of malarial parasites in blood preparations, or to undertake differential staining or polar staining in diphtheria bacilli or plague bacilli, can be obtained by immersing the smear for 15 to 20 minutes in absolute alcohol, in a mixture of alcohol and ether, or, best of all, for 3 to 5 minutes in absolute methyl alcohol, instead of passing through the flame.

Staining.—This is done by one of the methods described below, and the smear is then washed in water, under the tap, inclining the smear slightly, beneath a delicate stream, so as to protect the film as much as possible. If preferred, a chemical wash bottle may be used. If there be any doubt as to the film side of the preparation, it can usually be detected by scratching the surface with a pin.

The smear is next dried between folds of filter paper, several layers thick, the paper being pressed directly upon the smear and stroked gently until dry. The drying can be completed by holding the smear, film side up, high above a small flame.

The smear is now ready for microscopic examination with the oil immersion lens. If the smear has been made upon a slide, a drop of cedar oil is placed directly upon it, and the immersion lens run into it (open diaphragm); or a drop of neutral Canada balsam and a cover glass may be applied, pressed down gently so as to form a thin layer, after which a drop of cedar oil is placed on the surface of the cover slip before examination with the immersion. If the smear has been made upon a cover slip, this is mounted in a thin film of neutral Canada balsam, on a clean slide, and examined in the same way.

(*b*) *Examination of Unstained Fresh Preparations*

The infectious agent can often be seen in unstained fresh preparations of the material collected.

Thus, if *malaria* be suspected, a drop of blood taken from the ear, on an absolutely clean cover glass, may be placed upon an absolutely clean slide, when the drop will flatten out into a layer one corpuscle thick. (See Examination of Blood.) A drop of cedar oil is applied, and the examination made immediately with an oil immersion lens (medium or small diaphram). The pigment of the parasite may first catch the eye when the generation is near maturity. Young parasites are difficult to recognize at first, though with a closed diaphragm they may be recognized, especially the forms that show ameboid movements. Such an examination should always be supplemented by the study of a fixed smear, stained by Wilson's or Giemsa's method.

In pus from subcutaneous abscesses, if *blastomyces* (oidiomycosis) be suspected, the doubly contoured parasites are easily recognizable in the fresh slide.

If *amebic dysentery* be suspected, a particle of mucus from the stool can be examined fresh beneath the cover slip, on a warm slide and warm stage. The typical subdivision into ectosarc and endosarc, the active ameboid movement, and the phagocyted red corpuscles are characteristic.

(*c*) *Examination in Hanging Drop*

This is rarely used for the direct examination of material collected from the patient, but is very helpful for the study of particles of living cultures derived from such material.

The slide about the edge of the cavity in a hollow slide is surrounded with vaseline. With a sterile oese, a small drop of the culture is placed in the middle of a clean cover slip, lying on a piece of white paper, or a small drop of salt solution or sterile bouillon can be placed upon the cover slip and inoculated with a minute particle of solid material containing the bacteria, with a sterile platinum needle. The glass slide, with the cavity downward, is now laid upon the cover slip so that the drop comes directly in the middle of the cavity; it is then pressed gently into

the vaseline. The slide is next carefully turned over so that the cover glass is above, and the drop hangs from its under surface into the cavity.

The slide is now placed under the microscope. With the low power and closed diaphragm, the edge of the drop is first sought and brought exactly into the middle of the field. A drop of cedar oil is next applied to the cover slip, the diaphragm opened about 1/3, and the oil immersion fixed upon the edge of the drop. This found, the slide may be cautiously moved as the bacteria in the hanging drop are sought for and studied. The method is especially useful in studying motility.

4. Methods of Staining Bacteria and Parasites

The ordinary stains of the bacteriological laboratory are employed. The basic dyes, like methylene blue, gentian violet, and fuchsin, stain bacteria and cell nuclei intensively. Sometimes a contrast stain with an acid dye, like eosin, is also used.

The dyes are kept in 2 per cent aqueous solution, or, better, in 5 per cent alcoholic solution, to be diluted just before use with 4 to 10 parts of water.

(*a*) *General Stains*

i. Alkaline Methylene Blue (Loeffler)

The stain consists of 30 ccm. of a saturated alcoholic solution of methylene blue with 100 c.c. 0.01 per cent KOH.

ii. Carbol-Fuchsin (Ziehl-Neelsen)

The stain consists of 1.0 gram fuchsin, 5.0 acid carbol liq., 10.0 alcohol, 100.0 aqua distillata. The solution keeps well. If diluted 10 times it stains all ordinary bacteria in a few seconds. To stain tubercle bacilli it is applied in an especial way (*vide infra*).

iii. Anilin Water Gentian Violet (Ehrlich)

Five c.c. anilin oil are thoroughly shaken with 100 c.c. distilled water, and filtered through a moist filter. In the filtrate, 4 grams of gentian violet are dissolved. The solution is to be filtered again, just before use. The stain does not keep well, spoiling in two or three weeks. Instead of adding the crystals of gentian violet, 11 c.c. of a saturated alcoholic solution of gentian violet may be used.

iv. Wilson's and Giemsa's Stain (Methylene Azure and Eosin)

(See Staining of Blood Smears.)

These stains are especially useful for demonstrating malarial parasites, spirochætes, and trypanosomes.

(*b*) *Special Stains*

i. Gram's Stain

The method consists in staining the bacteria with gentian violet, and treating the smear with Lugol's solution, through which a union of iodin with the stain

occurs, after which the smear is washed in alcohol. Certain bacteria retain the stain and are called *Gram-positive;* others decolorize and are said to be *Gram-negative.*

Technic.—1. Stain with warm anilin gentian violet for two minutes.

2. Place in Lugol's solution (iodin 1, KI 2, distilled water 300) for from ½ to 2 minutes. The specimen turns black.

3. Wash in absolute alcohol until the color just ceases to be visible to the naked eye.

4. Counterstain with 2 per cent aqueous solution of Bismarck brown.

5. Wash in water, dry, and mount.

The Gram-positive bacilli will be stained violet; the Gram-negative bacilli will be stained brown.

Gram-positive Bacteria.—(1) Nearly all cocci (staphylo, strepto, pneumo) except gonococci and meningococci; (2) diphtheria bacilli; (3) anthrax bacilli; (4) tetanus bacilli; (5) tubercle bacilli; (6) lepra bacilli, etc.

Gram-negative Bacteria.—(1) Gonococcus; (2) meningococcus; (3) micrococcus catarrhalis; (4) typhoid bacillus, and paratyphoid bacillus; (5) influenza bacillus; (6) B. coli; (7) B. pyocyaneus; (8) B. mallei; (9) B. pestis; (10) cholera vibrio; (11) B. dysenteriæ; (12) Friedländer's bacillus; (13) whooping-cough bacillus (Bordet); (14) bacillus of soft chancre, etc.

ii. Stains for Tubercle Bacilli, and Other Acid-Fast Bacilli

These bacilli stain with difficulty, probably on account of the waxlike substance they contain. Once stained, unlike other bacteria, they hold the stain tenaciously, even in the presence of acid; they are *"acid-fast."* If a second dye be used as a counterstain, it will color the bacteria which are *"non-acid-fast."*

I. Method of Ziehl-Neelsen.—1. Stain for 1 to 2 minutes in concentrated carbol-fuchsin, heating until steam comes off.

2. Wash quickly in water.

3. Decolorize in 5 per cent H_2SO_4 for 2 to 5 seconds, or in 3 per cent HCl-alcohol, or in 30 per cent aqueous HNO_3 solution, for 1 to 3 seconds.

4. Wash in 70 per cent alcohol until almost colorless.

5. Rinse in water.

6. Counterstain with weak methylene blue solution, 5 to 10 seconds.

7. Wash again in water, dry, and mount.

All acid-fast bacilli, including tubercle bacilli, stain bright red; other bacteria, cell nuclei, and mucus, stain pale blue. Besides tubercle bacilli (human, bovine, avian, etc.), a number of other bacilli are acid-fast (pseudo tubercle bacilli, smegma bacilli, lepra bacilli).

II. Method of Fraenkel-Gabbett.—Here the decolorizing and counterstaining are done simultaneously. After staining in hot carbol-fuchsin, the specimen is rinsed in water and placed in the following solution: Methylene blue 2.0, acid sulphuric concentrated 25.0, alcohol 50.0, distilled water 100.0. It is left here about

5 minutes, until the preparation looks slightly blue. It is then rinsed thoroughly in water, dried, and mounted.

Either of the above methods is useful for staining tubercle bacilli in sputum, urine, feces, or cerebrospinal fluid.

III. Antiformin Methods.—These are used for demonstrating tubercle bacilli, present in small quantities, in blood, sputum, or tissue. The antiformin, which is a mixture of hypochlorit of soda and NaOH, quickly destroys all organic substances (including bacteria), except acid-fast bacteria, which still retain their form, vitality, and colorability. Urinary sediments containing tubercle bacilli, treated with antiformin and injected into guinea-pigs, cause infection, showing that the tubercle bacilli are not killed.

Several antiformin methods have been used. Uhlenhuth's seems as good as any. The material is dissolved up in an equal volume of 15–20 per cent antiformin solution by allowing the mixture to stand for 10-12 hours in the thermostat at body temperature. The tubercle bacilli can be obtained in concentrated aggregate by centrifugalizing. The centrifugate is used for staining, or for animal experiments.

A quick method has been introduced by Lorenz. From 2 to 10 c.c. of sputum are shaken in a test tube for about 5 minutes with two or three times as much 15 per cent solution of antiformin. The shaking is continued until the mixture is homogeneous, then boiled and strongly centrifugalized for about 15 minutes. The sediment is spread on a glass slide, diluted with a few oeses of water, dried, fixed in a flame, and stained.

Methods have been introduced for differentiating tubercle bacilli from other acid-fast bacilli (Korallin method, and House's method). For these, the special text-books must be consulted. They are not absolutely reliable, and, where there is doubt, cultures should be made, or animal inoculations undertaken.

iii. Stains for Treponema pallidum

The material can be obtained from a mucous patch in the mouth, from a hard chancre, or from other luetic lesions. In the case of hard chancre, the surface is first touched several times with a bit of cotton wet in ether, then cautiously scraped with a knife short of hemorrhage, after which a scraping is cautiously made from the middle to the periphery of the chancre until a little bloody serum just appears. It is well to examine a droplet of this fresh, by "dark-field illumination"; often the spirochætes can be seen in lively rotary motion. A drop is taken up with the edge of a thoroughly clean glass slide, or cover slip, and spread upon a similarly clean slide by stroking. If the smear be correctly made, single intact red corpuscles will be scattered in it. The smear is dried in the air and fixed in the flame in the ordinary way.

Methylene Azure Eosin.—The preparation is stained with Wilson's or Giemsa's stain (20 drops to 20 c.c. of water). Some of the diluted stain is placed on the slide, which is clean, warmed over the flame until steam arises, but short of boiling. The first stain is poured off and fresh stain added and heated, and this process repeated several times. The quicker the staining is carried on, the better. Wash in water, and dry. Red blood corpuscles and spirochætes are stained a bright red color and look granular.

India Ink Method.—A drop of serum obtained from the chancre as above described is mixed evenly with a drop of fluid India ink of the best quality on a glass

slide, after which an even thin smear is made with the end of another slide, or with the edge of a cover slip, allowed to stand ½ minute, and dried. Examine at once with oil immersion lens.

The spirochætes are seen as glistening, silverlike cork-screws, lying on a homogeneous brown background. This method can be warmly recommended for clinical diagnosis.

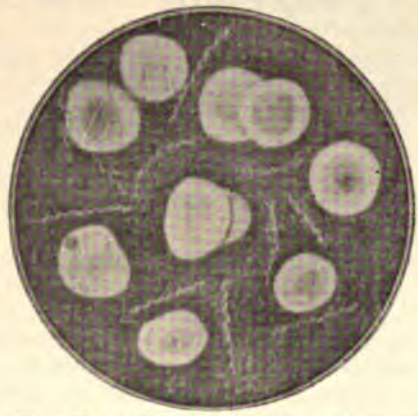

Fig. 51.—India Ink Preparation from a Luetic Papule—Papulopustular Syphilide in an Infant. (After E. Moro in E. Leer's "Lehrb. d. Kinderheilkunde," published by G. Fischer, Jena.)

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iv. Stains for Capsules

Several methods are in use. Two of the better known stains will be given here.

Welch's Method.—After fixation, place a drop of glacial acetic acid on the smear. After a few seconds pour off the acid and cover smear with anilin, water gentian violet, renewing the stain several times. When staining is complete (3-5 minutes) wash preparation in 2 per cent salt solution and examine in this solution.

Johne's Method.—1. Stain with 2 per cent aqueous solution of gentian violet, warming for 2 minutes.

2. Wash in water, decolorize in 1 to 2 per cent acetic acid for 6-10 seconds.

3. Wash in water and examine in the same. (In Canada balsam the capsules disappear.)

v. Stains for Spores

Moeller's method is often used. Fix a cover slip in the ordinary way, and immerse for from 5 seconds to 10 minutes in 5 per cent solution of chromic acid, the time varying for the different varieties of bacteria, and to be tested in each case. Wash in water, stain in steaming carbol-fuchsin 1 minute, decolorize for 5 seconds in 5 per cent H_2SO_4, wash in water, counterstain with aqueous methylene blue solution, wash, dry, mount. The spores will be stained red, the bodies of the bacteria blue.

Another method consists in placing some of the material in ½ c.c. salt solution, and adding to this ½ c.c. filtered carbol-fuchsin solution. Place the test tube in boiling water for 10 minutes. Place a droplet on a glass slide and warm. When dry, fix in the flame and decolorize in equal parts of absolute alcohol and water

(if necessary, acidulating with HCl); wash in water; counterstain with Loeffler's methylene blue.

vi. Stains for Flagella

I. Bunge's Method.—With the point of a platinum needle, place a minute particle of a young agar-slant-culture (not bouillon culture) in a small droplet of water on a cover slip. Mix well, make a smear, dry quickly. Immerse the cover slip in Bunge's mordant (25 c.c. of a 25 per cent ferric chlorid solution, plus 75 c.c. saturated solution of tannic acid) for 1 minute, heating until steam comes off. Wash in water and dry. Float on carbol-gentian-violet, and warm gently. Wash in water; dry; mount in balsam.

II. Zettnow's Method.—SOLUTION A.—10 g. Tannin dissolved in 150 c.c. distilled water.

SOLUTION B.—Tartar emetic 2 g. dissolved in 40 c.c. hot distilled water.

Warm A. to 40° C. (not above 45° C.); to it add gradually 27-28 c.c. of Sol. B., or until the precipitate which arises does not materially diminish after a few minutes' shaking. This mordant is ready for use at once and can be kept for months by adding a large thymol crystal.

TECHNIC.—Place some of the mordant in a test tube after shaking the flask well. Boil until clear. Lay the cover slip in a box-glass with the film side down, and pour the warm mordant over it. Leave the cover slip in until the cooling mordant begins to become turbid; then remove the cover slip and wash with water; then fasten it in a Cornet forceps and set on edge to drain and dry. Now lay the cover slip horizontally and cover it with a solution of methylamine silver made by shaking 2-3 grams silver sulphate violently with 200 grams water until saturated. Of this solution, one part is diluted with 1 part distilled water, and then mixed with 33 per cent methylamine solution until the precipitate first arising again dissolves. Warm the cover slip, covered with silver solution, in a low flame until vapor begins to come off; wash with water, and dry. The silver sulphate is made by precipitating silver nitrate solution with magnesium sulphate or sodium sulphate.

The flagella are stained black; in many bacteria they are attached all around the body of the bacterium (*peritrichous*); in others, there is only a single flagellum at one end (*monotrichous*).

5. Bacterial Cultures for Clinical Diagnosis

Both fluid and solid media are used. Among the fluid media, *bouillon*, plain or enriched, and *peptone solution* are most employed. For the isolation of typhoid bacilli, *Conradi's bile medium* (ox bile 900 c.c.; glycerin 100 c.c.; peptone 20 grains) is often used. *Plain milk* and *litmus milk* are also valuable for differential diagnosis.

Among the solid media, coagulated *blood serum*, especially Loeffler's serum, to which 1 per cent glucose bouillon has been added, is much used, for the isolation of diphtheria bacilli. *Potato*, *gelatin*, and especially *agar*, either plain, or agar to which glycerin, blood, glucose, or other substances have been added are in daily use.

Reliable media can now be purchased. If one makes one's media, it

may be convenient to use instead of agar, the so-called ragit (Merck), which simply needs to be dissolved up to be ready for use.

Certain special media have been found useful in making cultures from stools when it is desired to isolate typhoid, paratyphoid and colon bacilli. Several of the more important follow.

Lactose-litmus-nutrose agar (Drigalski and Conradi), by means of which we find out whether a bacterium can decompose the milk sugar with formation of acid which reddens litmus. The medium should be prepared as directed in Hiss and Zinsser's Text-book. In addition to litmus and lactose it contains crystal violet to inhibit the growth of bacteria other than B. typhosus or B. coli. On this medium, typhoid bacilli, paratyphoid bacilli (A and B), and dysentery bacilli, grow as blue colonies, while the colon bacillus grows as red colonies.

Fuchsin-sulphite agar (Endo). To a liter of 3 per cent neutral agar are added 10 c.c. of 10 per cent soda solution, 10 g. lactose, 5 c.c. saturated fuchsin solution (filtered); then add 25 c.c. freshly prepared solution of sodium sulphite (10 per cent). This medium is clear when the reaction is alkaline and sodium sulphite is present. It should be kept in the dark, and air-tight. For use, it is poured into Petri dishes.

Bacteria that convert the milk sugar into lactic acid grow as red colonies, while other bacteria form colorless colonies. Endo's fuchsin agar can be prepared quickly by the use of the so-called Endo-capsule (Merck).

Malachite-Green Agar.—This consists of 3 per cent neutral agar plus 5 c.c. normal NaOH (per liter) plus 1 per cent nutrose plus 1 c.c. of a 1 per cent solution of malachite green (C. P. Hochst) in water and alcohol. According to H. Schindler, it is best to make tests with varying amounts of malachite green in the medium until one gets the composition in which most typhoid colonies and fewest colon colonies will grow. The medium has the advantage of inhibiting the growth of B. coli and various other bacteria.

Hints for Culture.—For the diagnosis of diphtheria, slants of Loeffler's medium are very satisfactory. For blood and sputum cultures, blood-agar Petri plates are desirable. For cultures from the stools, the special media of Drigalski and Conradi, Endo, etc., are useful.

For the exact determination of the bacterial species obtained, all the ordinary methods of the bacteriological laboratory must be employed in the clinical laboratory (blood cultures, surface cultures on various media, animal experiments, etc.).

If the presence of *anaërobic* bacteria be suspected, oxygen-free growth should be attempted (pyrogallic acid method; hydrogen or illuminating-gas method; mechanical method; plastillin method of Lentz and Heim). (See Special Texts.)

In studying the *biological properties* of bacteria, the capacity for fermentation of sugars and proteins, for the formation of alkali or acid, H_2S or indol, the oxygen-need, the reducing capacity, the toxin production, and the production of pigment, may need investigation.

The value of blood-cultures is often so great from a diagnostic point of view that it is a pity that they are not more often made outside of the hospitals. Satis-

factory blood-cultures can be made by any physician who has had elementary training in bacteriology, though he may require the assistance of a trained laboratory worker in the interpretation of the results.

The patient's arm is thoroughly washed with green-soap followed by 70 per cent alcohol. An Esmarch bandage, or a length of rubber tubing, is applied about the upper arm tightly enough to cut off the venous flow but not to obliterate the radial pulse. The veins of the forearm are thereby distended and show prominently. In fat people, in women, and in cachectic patients, this maneuver may not suffice to render the veins visible. They must then be palpated by passing the fingertips gently across the forearm. The veins are readily felt as cords in the subcutaneous tissues. If the patient clench and unclench the fist the veins often become more prominent. In very difficult cases immersion of the arm in hot water (with the bandage on) will often be of use. As a rule, no difficulty is experienced in finding a suitable vein. The easiest to enter with a needle are not the most superficial veins, but those whose attachment to the deep fasciae renders them less mobile—a point on such a vein is hence selected. If palpation has been necessary, the skin is again cleansed with alcohol. Keep the patient's fingers and flies off this prepared area. Nothing should touch the needle nor the skin where the needle is to enter.

A 10-20 c.c. Luer, or Record syringe with a sharp needle (No. 18-20) and a hemostat should meantime have been boiled for three minutes in a shallow pan. (Caution: remove the piston for boiling). The water is carefully drained off. The barrel is picked out, the piston fitted into it, and then with a sterile hemostat the needle is picked up and fitted on and the obturator gently pulled out from the lumen of the needle.

The point of the needle is then passed through the skin overlying the vein, with a quick thrust, and then more slowly it is pushed through the wall of the vein itself. In this way one avoids passing completely through the vein. When the point of the needle enters the lumen of the vein, blood mounts into the syringe. The piston is slowly drawn out until the requisite amount of blood is obtained. If the flow becomes very slow it is best to stop, as too great delay at this stage will result in clotting inside the syringe. Ten c.c. are sufficient. The constrictor is loosened before the needle is withdrawn. The cotton stopper of a tube of media is then flamed over an alcohol lamp, withdrawn and held between two fingers, the mouth of the tube flamed, and the proper quantity of blood delivered into the media, after which the tube is plugged. Each tube or flask of media is thus rapidly inoculated in succession. If desired, some of the blood may be placed in an empty tube for the Wassermann or Widal test. The syringe should be washed with cold water before clotting in the barrel occurs.

Since outside hospitals it is often awkward to melt down agar, and to pour plates, reliance is usually placed upon the liquid media of which the various bouillon and bile medias are the standbys. It is probably better to deliver the blood from the syringe into a small sterile flask, containing a few c.c. of sterile 1 per cent sodium citrate to prevent coagulation. The flask is then taken to the laboratory where transfers to suitable media are made.

Recently, there have been placed upon the market vacuum tubes (Keidl) containing sterile citrated-glucose-bouillon. A needle and rubber connection are furnished, which are boiled and then fitted over the point of the vacuum tube. The needle is introduced into the vein and the fine point of the tube broken by bending the rubber connection. The vacuum draws blood into the citrated media. The tube can then be taken to the laboratory. Empty tubes may be used for collecting blood for the Wassermann test.

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6. Animal Inoculations, and Virulence Tests

Subcutaneous, intravenous, intraperitoneal and subdural injections of the bacteria under examination may be necessary, especially in testing virulence. Certain bacteria are virulent for certain animals, not for others, a point often useful in diagnosis.

In a number of instances, bacteria can be most easily isolated in pure culture by passing the material through a susceptible animal. This is especially true of the bacillus of tetanus, the tubercle bacillus, the anthrax bacillus, and the pneumococcus.

If sputum contain the *pneumococcus,* a small portion of it placed under the skin at the root of the tail of a mouse will lead quickly to the death of the animal, and the pneumococcus can be obtained in pure culture from the heart's blood. If a few cubic centimeters of the blood of a human being suffering from lobar pneumonia be injected into the ear vein of a rabbit, the rabbit will often die within 24 hours, and enormous numbers of pneumococci in pure culture can be found in the heart's blood.

If the centrifugate of the urine, in a case of renal *tuberculosis,* be injected into the peritoneum of a guinea-pig the animal may be killed at the end of 2 or 3 weeks and tuberculous lesions found, from which tubercle bacilli may be grown in pure culture.

Rats are very susceptible to plague; *rabbits* to staphylococci, streptococci and pneumococci; *dogs* to malignant edema; *guinea-pigs* to tuberculosis and glanders; *mice* and *rats* to anthrax.

For details of animal inoculations special text-books on bacteriology should be consulted.

D. Clinical Applications of Immunological Methods

The newer knowledge of immunity and anaphylaxis (allergy) has already been utilized in clinical diagnosis, especially in certain serodiagnostic reactions.

Among the antibodies utilized for clinical diagnostic tests are (1) agglutinins, (2) lysins, (3) precipitins, (4) opsonins, and (5) ergins. The principles underlying these tests have been described above. Here the technic of some of the tests themselves will be given.

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1. Tests for Agglutinins

Agglutination reactions may be employed either for the *identification of a given organism* (with an immune serum) or for the *recognition of the nature of an immune serum* (with a known bacterium). Thus, in the former instance, an emulsion of an unknown bacterium is treated with diluted immune serum (antityphoid, anticolon, antidysentery, etc.); in the latter instance the unknown serum is tested against a series of known bacteria. The most important clinical agglutination reaction is the so-called **Widal reaction** in typhoid fever, though the same principle has also been utilized for diagnostic purposes in paratyphoid, in meningococcus infections, and in Malta fever.

(*a*) *The Widal Reaction*

This may be carried out by the microscopic or by the macroscopic method. For the former, only a few drops of blood are necessary; for the latter 1–5 c.c. are desirable. In addition, known typhoid bacilli of agglutinable strain must be available, preferably an 18 to 24-hour old bouillon culture, or a thin suspension of bacilli made by rubbing up a small loop of the growth, from an 18-hour agar culture, in 5 c.c. of sterile 0.8 per cent NaCl solution.

Microscopic Test.—The examination is made in the hanging drop (see above). The serum is diluted, first with 24 parts of salt solution by means of a mixing pipet, and from this other dilutions —1:50, 1:100, and 1:200— are prepared. A drop of each dilution—1:25 to 1:200—is placed upon a cover slip by means of a platinum loop, and a small drop of the fresh bouillon culture, or agar growth in suspension added. The vaselined hollow slide is then applied, and the specimens examined at once, with a high-power dry lens. If large clumps of bacteria are visible, the preparation is discarded, and the suspension of bacilli centrifugalized for a minute or two. This throws any clumps to the bottom, and the supernatant fluid may be used for making new preparations. When satisfactory specimens, free from clumped organisms, have been obtained, they are set aside for from ½ to 1 hour and then re-examined. If the reaction be positive, the bacilli will have lost their motility, and will be

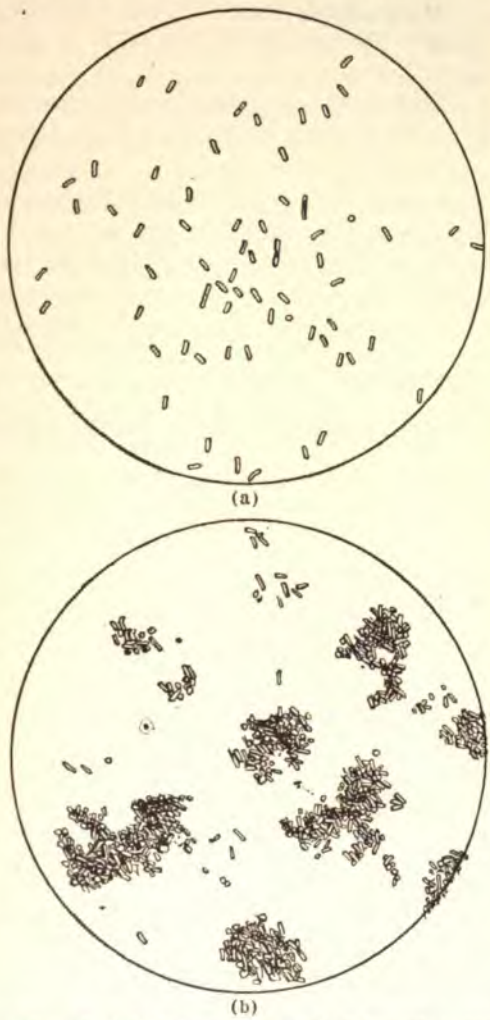

Fig. 52.—Widal Reaction—Half Schematic; (a) Typhoid Bacilli Free; (b) Typhoid Bacilli Agglutinated. (After H. Schottmüller in Mohr and Staehelin's "Handb. d. inner. Med.," published by J. Springer, Berlin.)

ıuch a long period, persistent local infections (bones, gall-blad-
· be suspected. Probably all typhoid carriers yield a positive
ıction.
l be interesting to learn how long the Widal reaction remains posi-
prophylactic inoculation against typhoid.
.rallelism exists between the severity of the case and the amount
nins formed.
nteresting that some strains of typhoid bacilli yielding a negative
lilutions of 1:50 and 1:100 yield a definitely positive result in
utions (1:500; 1:1000).
es of **group reaction,** one may determine the agglutination titer
ɔrganism of the group, or one may adopt Castellani's method of
portion of immune serum with each of the members of the group,
ılizing, and testing the supernatant fluid for its agglutination
he other members. (For References, see pp. 121-122.)

'ests for Lysins (Bacteriolysins; Hemolysins)

ıbstances concerned have already been described. Two main clin-
:ations are used: (a) Pfeiffer's experiment, and (b) complement
:sts.

(*a*) *Pfeiffer's Experiment*

nmune serum from the rabbit (against cholera or typhoid) be inactivated
d injected, with its corresponding (homologous) bacteria, into the peri-
ty of a guinea-pig, and a little of the peritoneal exudate obtained by
ne glass capillaries be examined at intervals (immediately, after 5 min-
ıinutes, 30 minutes, etc.) in hanging drop preparations, it will be
ıat the bacteria quickly lose their motility, swell up, become granular, and
.arters of an hour or an hour are completely dissolved (*bacteriolysis*).
:ment of the guinea-pig's peritoneal fluid has reactivated the amboceptors
.une serum and caused bacteriolysis.
ıction is strongly specific, and is of great importance, especially in the
f cholera, when it is desirable to establish without doubt the diagnosis in
:es of the disease at the beginning of an epidemic by isolating the cholera
ıltures and establishing the identity of the cultivated vibrio.
:is of an Unknown Bacterium by Bacteriolysis with a Known Immune

Guinea-pig B receives 10 times the titer dose, i. e., 2 mg. of an immune serum with a titer of 1:5000.

Guinea-pig C, a control animal, receives 50 times the titer dose, i. e., 10 mg. of normal rabbit's serum.

The serum injected into the peritoneal cavity of each of these three animals is first mixed with 1 oese of an agar culture of the suspected bacterium (18 hours at 37° C.) rubbed up in 1 c.c. bouillon (not in salt solution or peptone water).

Guinea-pig D receives 1 oese of the bacterial culture in 1 c.c. bouillon, without other admixture, in order to find out whether the culture is virulent for the guinea-pig or not.

If, in the first two animals, A and B, bacteriolysis occur within 20 minutes, or at the latest within one hour, while in animals C and D, bacteriolysis has not occurred, the reaction is positive, and the microörganism is proven to be the suspected infectious agent.

Diagnosis of an Unknown Immune Serum by Bacteriolysis of a Known Bacterium.—One can, on the other hand, use the same principle for determining whether a serum derived from a patient suspected to have typhoid or cholera, or from a convalescent from these diseases, contains immune bodies (bacteriolysins against the typhoid bacillus, or against the cholera vibrio). The suspected serum (usually in dilutions of 1:20, 1:100, 1:500) is injected, together with the bacteria, into the peritoneal cavity of the guinea-pig; examinations are made, at intervals, up to 1 hour, to see whether the organisms undergo granular disintegration and lysis.

Bacteriolysis in Vitro.—The method described above requires a living animal; the test is done *in vivo*. It can also be carried out *in vitro* (Stern and Korte). Inactivated typhoid serum (in different dilutions) is mixed in test tubes with serum containing complement (fresh rabbit serum) and with known typhoid bacilli; the mixture is allowed to stand for 45 to 60 minutes, after which agar plates are made to determine in what dilutions the serum has killed, or markedly diminished, the growth as contrasted with the control tests in which inactivated normal serum was used instead of immune serum. In typhoid fever, positive results are usually obtainable with dilutions of 1:1000, and even in less concentration.

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NOTE.—For other references, see pp. 116–118.

(*b*) *Complement Fixation Tests*

As has been fully described above, by *complement fixation* is meant the fact that when antigen and specific antibody are mixed together, the complement present becomes anchored, so that no complement is available for an introduced hemolytic system (hemolytic amboceptor + red corpuscles), and no hemolysis results.

Complement is fixed in the presence of amboceptor and bacterial antigen (Bordet-Gengou phenomenon); it is also fixed in the presence of pre-

cipitin and protein-antigen (Gengou-Moreschi phenomenon). Both these forms of complement fixation have been used in clinical diagnosis.

If one immunize a large rabbit by injecting it on several (3–4) occasions, 4–6 days apart, with the washed corpuscles from 1.0–10.0 c.c. of sheep's blood (asepsis!), the rabbit's serum in 10–12 days after the last injection will possess in favorable cases a strong specific hemolytic power for sheep's corpuscles, the hemolysis depending upon the coöperation of two substances, (1) specific hemolytic amboceptor, and (2) non-specific normal complement.

If such an immune serum be rendered inactive by heat, it will still contain hemolytic amboceptor but no complement.

Now, if a given antigen be mixed with the (homologous) amboceptor to which it can, on injection, give rise, the two unite to form a compound which has an extraordinary affinity for free complement; the compound formed by their union binds the complement firmly, while either antigen or amboceptor alone possesses only slight affinity for such complement. If one suspect that a patient's serum contain a certain specific amboceptor, and, to a portion of this serum, some corresponding antigen (extract of syphilitic liver, typhoid bacilli, etc.) be added, together with a little fresh complement, and the whole be kept at 37° C. for a short time, the *complement will be bound (fixed, or anchored)*, if the suspected amboceptor be present. Now, since in this fixation all free complement has been used up, if the hemolytic system be introduced (sheep's red corpuscles + hemolytic amboceptor in the form of inactivated immune serum), no hemolysis will occur because of the lack of free complement (*positive reaction for complement fixation*); but should we be wrong in our surmise regarding the presence, in the patient's serum, of an amboceptor corresponding to the antigen used, the complement will not be bound, and so free complement will be available to activate the hemolytic amboceptor, and the red corpuscles of the hemolytic system will be laked; in other words, hemolysis will occur (*negative reaction for complement fixation*).

The method has been used for the diagnosis of typhoid fever, of tuberculosis, of chronic gonorrhea, and of certain other infectious diseases, but it has scored its greatest triumph in the serum diagnosis of syphilis, for which purpose it was applied first by Wassermann, Neisser and Bruck (1906), the test being generally known as the **Wassermann reaction.** They used an extract of the liver of a luetic fetus as antigen. About the same time, Detre used as antigen an extract of condylomata.

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i. Wassermann Reaction (Wa.-R.)

It was first shown that the serum of syphilitic patients, mixed with salt solution extracts of syphilitic organs (liver of congenital syphilis) as antigen, would absorb complement. From this it was assumed that the salt solution extract of luetic organs contains syphilitic antigen, and also that the blood serum of syphilitic patients contains specific (syphilitic) antibodies (amboceptor).

It turns out from later studies that alcoholic extracts and acetone extracts of luetic liver work as well as saline extracts, and, moreover, extracts from perfectly normal tissues (human heart, guinea-pig's heart) work as well as those from syphilitic organs, especially if a little cholesterin be added.

The antigen appears to be a lipoid body, possibly related to lecithin, and the antibody in the serum of syphilitic patients can scarcely be an amboceptor in the sense of Ehrlich, but seems rather to be some substance with a marked affinity for lipoid bodies. It has been called the lipoidophilic antibody (C. E. Simon).

As a *hemolytic system,* sheep's corpuscles, together with the antiserum made by injection of sheep's corpuscles into rabbits and inactivated by heat so as to contain only amboceptor, was used, and, for *complement,* fresh guinea-pig's serum was employed.

Before carrying out the test, certain control experiments must be made to determine the activity of the extract, of the hemolysin, and of the complement, and to make sure that the serum to be tested does not, of itself, inhibit hemolysis (*autotropic serum*).

Technic.—The five substances necessary for the test are (1) the antigen, (2) the serum suspected to contain the amboceptor corresponding to the antigen, (3) complement, (4) hemolytic amboceptors, (5) corresponding red corpuscles.

1. The ANTIGEN, as originally obtained, is a watery extract made as follows: A weighed amount of the liver of a macerated syphilitic fetus is cut into small pieces, ground up, shaken for 24 hours in 4 times its weight of salt solution (0.85 per cent) containing 0.5 per cent carbolic acid, the coarser particles removed by a gauze filter, and the mixture briefly centrifugalized (half a minute). The centrifugate thus obtained is not a solution, but a homogeneous, fairly stable suspension. It is kept in a dark flask, in the ice-box, and should always be well shaken before using. The amount of extract necessary to combine complement is determined in a preliminary experiment, and it is also ascertained whether the extract alone will hemolyze red blood cells without the presence of either complement or hemolysin. Practically, only those antigens are used of which 0.4 c.c. will not of itself fix the complement.

Many workers use, instead of the above watery extract, an *acetone extract,* made by extracting 1 gram dried substance of luetic liver, normal heart or guinea-pig's heart, rubbed up in a mortar with pure acetone. The suspension is placed for 8-10 hours in the thermostat at 37° C., and then for the same length of time in a shaking machine, after which it is allowed to stand half a day at the room temperature, and then filtered. The flask should be closed air-tight with a rubber stopper.

Extracts (aqueous or acetone) must be tested out to see (1) whether they are suitable for the Wassermann reaction, and (2) if found suitable, what amounts it is best to use to secure reliable results.

Noguchi has prepared an antigen by using the *acetone-insoluble fraction of alcoholic extracts,* since he has found that the antigen thus prepared is free from the decomposition products of protein, such as albumoses and peptones, which are capable of "proteotropic ferment fixation." The heart, liver or kidney of man or animal is hashed and extracted with 10 volumes of absolute alcohol for several days at 37° C. This extract is filtered, the filtrate evaporated *in vacuo* to dryness, extracted with ether, the ethereal extract concentrated, and mixed with 10 volumes of pure acetone. The insoluble precipitate is collected, dissolved in a minimal amount of absolute methyl alcohol, and kept in ampules as a stock solution. For use, enough stock solution is dissolved in salt solution to make a solution containing 0.3 per cent of the original lipoids. This can be kept on ice until it is used.

Noguchi has also prepared an *antigen from pure cultures* of Treponema pallidum.

Very recently antigens made of *alcoholic extract of beef-heart* to which 0.05 per cent *cholesterin* is added, have come into use. Such cholesterinized alcohol-extract antigens promise well. They may come into general use.

In such *testing of antigens,* we make use of a positive standard serum (luetic) and of a negative standard serum (non-luetic), controlled just before testing by a reliable standard antigen extract. We also control all the reagents (sera and extracts) individually with the hemolytic system,

to see if any one of them, with double the amount used in any test, will by itself inhibit hemolysis. Rough tests are first made for orientation with 5 doses of the extract (0.2; 0.1; 0.05; 0.025; 0.0125). If we find, for example, that the extract tested works well in the amounts 0.05 and 0.025, we then make tests of the efficiency of the extract in comparison with that of a well-tested standard extract, and raise and lower the dose of the new antigen until results are reached that are, as near as possible, like those obtainable with the standard antigen. The amount of new extract that does this is used as the ordinary dose. The extracts remain fairly constant in activity, so that the dose, once determined, can be relied upon as correct for a considerable period. Antigen when added to a hemolytic system in sufficient concentration will inhibit hemolysis. Since this effect is produced by the action of the concentrated antigen upon the complement it is spoken of as the *anticomplementary property* of the antigen. In titrating the antigen we observe, in the series with normal serum, whether any anticomplementary action is observable and what is the least concentration of antigen which will produce such an effect. In the positive-serum series we observe what is the smallest amount of antigen that will cause complete inhibition of hemolysis; this amount is usually spoken of as one *unit* of antigen. Double this amount (e. g., two units) should not be a sufficient amount to cause any anticomplementary action: and if it does the antigen should be discarded as unreliable.

2. The SERUM of patients suspected to contain syphilitic antibody is heated in small test tubes for half an hour at 56° C. As controls, sera from healthy patients are used.

Anticomplement may develop in sera that have stood for some time; it is destroyed by heat. Blood drawn after meals may be rich in anticomplementary substances. For this reason it is best to draw the blood for a Wassermann reaction before a meal.

Cerebrospinal fluids may be tested in the same way as serum. They need not be inactivated before use; indeed, as far as the complement itself is concerned, serum need not be inactivated, if acetone extracts be used (Noguchi), but in order to get rid of certain other substances it is best to heat the sera.

3. As COMPLEMENT, fresh guinea-pig's serum is used, diluted 1:10 with salt solution. The guinea-pig is bled from the carotid artery. The clot is broken up with a glass rod during its formation, and the whole quickly centrifugalized. Fresh serum can thus be obtained in a few minutes.

Instead of sacrificing a guinea-pig each time complement is desired, if only a little be required, it can be obtained by anesthetizing the animal and drawing off 3–5 c.c. directly from the heart by means of an aspirating needle.

Serum over 24 hours old should never be used.

4. For HEMOLYTIC AMBOCEPTOR the inactivated serum of a rabbit that has been immunized against sheep's corpuscles by 3 injections 5 days apart into the ear vein, or intraperitoneally, first with 2.0 c.c. concentrated red corpuscles, second with 1.5 c.c. of equal parts of corpuscles and salt solution, and third with 1.0 c.c. of a mixture of equal parts of corpuscles and salt solution, is used. Dick advises 3 c.c. of blood at the first injection, 6 c.c. at the second, 10 c.c. at the third, 15 c.c. at the fourth, and 20 c.c. at the fifth; the injections are then given 5 days apart.

This hemolytic serum must be *titrated* before use. We prepare a series of solutions varying in strength from 1:500 to 1:3000 and test 0.25 c.c. of each dilution with 0.25 c.c. of complement (1:10), and 0.25 c.c. of sheep's corpuscles (5 per cent). The amount of fluid in each tube is brought up to 1.25 c.c. with salt solution. The titer of the amboceptor should be at least such that 0.5 c.c. of a 1:2000 dilution (in salt solution) will completely hemolyze 0.5 c.c. of a 5 per cent suspension of washed sheep's corpuscles in the presence of 0.5 c.c. of a 1:10 dilution of guinea-pig's serum (complement) within 30 minutes at 37° C. This hemolytic serum after inactivation may be kept on ice in small sterile tubes.

5. The SHEEP'S CORPUSCLES are obtained from defibrinated sheep's blood (taken either from the ear, or, through a needle or cannula, from the V. jugularis, into a sterile flask containing glass pearls), centrifugalized, and then washed and centrifugalized three times with salt solution. The last centrifugate is drawn up with a graduated pipet and mixed with 19 volumes of 0.8 per cent salt solution so as to make a 5 per cent suspension of corpuscles. Since the blood of the sheep varies somewhat, and the fragility of the corpuscles is sometimes increased, the preliminary hemolytic experiment (q. v.) is needed as a control of the sheep's corpuscles, as well as to inform us about the laking power of the amboceptor used.

Preliminary Hemolytic Experiment

This experiment (see below) is for the purpose of establishing the strength of the hemolytic system to be chosen; that is, the amount of amboceptor necessary for the actual experiment. The amount may vary, because the content of a guinea-pig's serum in active complement varies considerably. The poorer a guinea-pig's serum is in complement, the greater the amount of amboceptor that must be added to make sure that a part of the corpuscles will not remain unaltered.

The task of this preliminary experiment is then to establish the simple laking dose of the amboceptor, by which is meant the smallest amount of amboceptor that, along with 0.5 c.c. of complement in 1:10 dilution, is able completely to lake 0.5 c.c. of 5 per cent suspension of sheep's corpuscles ...nding 1 hour at the body temperature. At the end of an hour, one ...f the tubes, *a*, *b*, or *c*, is completely laked. Since *d* and *e*

PROTOCOL OF PRELIMINARY HEMOLYTIC EXPERIMENT

a	*b*	*c*	*d*	*e*	Remarks
0.5 NaCl **1**	0.5 NaCl **2**	0.5 NaCl **3**	....	....	NaCl = 0.85 per cent solution of NaCl.
0.5 stock solution of hemolytic amboceptor added, mixed, and 0.5 of mixture transferred to $b = \frac{1}{5}$. **4**	0.5 from *a* added, mixed, and 0.5 transferred to $c = \frac{1}{4}$. **5**	0.5 from *b* added, mixed, and 0.5 removed = $\frac{1}{8}$. **6**	....	....	....
1.0 NaCl. **7**	1.0 NaCl. **8**	1.0 NaCl. **9**	1.5 NaCl. **10**	2.0 NaCl. **11**	....
0.5 complement. **12**	0.5 complement. **13**	0.5 complement. **14**	0.5 complement. **15**	....	Complement is guinea-pig's serum (1 part) diluted with 9 parts salt solution.
0.5 sheep's corpuscles. **16**	0.5 sheep's corpuscles. **17**	0.5 sheep's corpuscles. **18**	0.5 sheep's corpuscles. **19**	0.5 sheep's corpuscles. **20**	Sheep's corpuscles = 5 per cent suspension of washed corpuscles = 1 c.c. of corpuscles mixed with 19 c.c. salt solution.

The tubes are well shaken and placed for 1 hour in the thermostat or 30 minutes in a water bath at 37° C.

contain no amboceptor they should show no laking; *d* is to prove that the complement does not of itself lake red corpuscles, and *e* to prove that the corpuscles are suitable and the salt solution isotonic.

In the protocol, the successive steps of the technic of the experiment are numbered in **blackface** type.

The Principal (Diagnostic) Experiment

After the preliminary hemolytic experiment has been carried out as above, we can proceeed to the making of an actual test, or the so-called Principal or Diagnostic Experiment. The following is the Wassermann System now in use in the bacteriological division of the laboratory of the Medical Clinic at the Johns Hopkins Hospital (Dr. Arthur Bloomfield in charge at time of writing).

REAGENTS:

1. Salt solution (.85 per cent).
2. Sheep's red blood corpuscles (5 per cent suspension).
3. Patient's serum (diluted 1:5 with salt solution and inactivated).
4. Antigen (previously titrated and used in less than one-half the anticomplementary dose). Two varieties of antigen are used for each test.
5. Complement (fresh guinea-pig serum, diluted 1:10 with salt solution).
6. Antisheep rabbit's immune serum (containing hemolytic amboceptor against sheep's blood).

TECHNIC (see Protocol):

Three tubes (I, II and III) are introduced as *general controls.*

Tube I contains only salt solution and corpuscles.

Tubes II and III both contain the hemolytic system with one of the two antigens used in double the amounts used in the test.

There are three tubes (1, 2, and 3) for each patient.

Tube 1 contains only the hemolytic system, with double the amount of patient's serum used in the test. This is the anticomplementary control for patient's serum.

Tubes 2 and 3 are the actual "test" tubes; each, however, contains a different antigen.

The total volume of fluid in each tube is 1.25 c.c.

The complement, and hemolytic serum have been titrated in the Preliminary Hemolytic Experiment.

PROTOCOL OF THE PRINCIPAL OR DIAGNOSTIC EXPERIMENT

	Tube No.	Salt Sol.	Antigen	Patients' Serum	Complement	Hemolytic Serum	Corpuscles	Total Vol. of Tube
Salt sol. and corpuscle control....	III	1	...	...	...	...	.25	1.25
Control for antigen A.....	II	...	.5 A	...	.25	.25	.25	1.25
Control for antigen B.....	I	...	.5 B	...	.25	.25	.25	1.25
Patient A.....	*1*	...	...	.5	.25	.25	.25	1.25
(Known positive.)	2	...	.25 A	.25	.25	.25	.25	1.25
	3	...	.25 B	.25	.25	.25	.25	1.25
Patient B.....	*4*	...	...	.5	.25	.25	.25	1.25
(Known negative.)	5	...	.25 A	.25	.25	.25	.25	1.25
	6	...	.25 B	.25	.25	.25	.25	1.25
Patient C.....	*7*	...	...	.5	.25	.25	.25	1.25
(To be tested.)	8	...	.25 A	.25	.25	.25	.25	1.25
	9	...	.25 B	.25	.25	.25	.25	1.25

Incubate * at 37° for ½ hour. Incubate * at 37° for 1 hour.

* Water bath.

Results: Tube III should show no hemolysis.
Tubes II and I should be completely hemolyzed; i. e., the antigen is not anticomplementary in double the amount used in the test.
Tubes *1*, *4*, 7, etc., should be completely hemolyzed; i. e., the patient's serum is not anticomplementary in double the amount used in the test.
Tubes 2, 3, 5, 6, 8, 9, etc., will, or will not, be hemolyzed, depending upon whether, or not, the complement has been fixed.
Hemolysis = no fixation = negative test.
Absence of hemolysis = fixation = positive test.

Since human serum may sometimes contain antisheep amboceptors, a negative reaction may be obtained, even though much complement is fixed. To guard against this, such natural antisheep amboceptor may be removed by Simon's method:

C. E. Simon's Method of Removing Antisheep Amboceptor.—To remove any natural antisheep amboceptors from the blood, Simon dilutes the inactivated serum with 5 volumes of a standard sheep's-corpuscle emulsion, inactivates for 30 minutes in the water bath, and then removes the amboceptor-laden corpuscles by centrifugalization. Any complementoid that may be simultaneously present is then gotten rid of at the same time (in the presence of natural antisheep amboceptors). After centrifugalization, the supernatant fluid is pipeted off and combined with the various reagents in the usual manner.

Noguchi's Method of Avoiding Negative Reactions Due to the Presence in the Human Serum of Antisheep Amboceptor.—For this purpose, Noguchi advises the use of a human hemolytic system instead of the sheep hemolytic system of the original Wassermann reaction. The full details of the method are to be found in Noguchi's book, and also in Ralph Webster's *Diagnostic Methods*. Webster uses this method as a routine, and asserts that, in his experience, "it is somewhat more reliable than the original Wassermann test in obscure cases." (See following table.)

Condition	Number of Cases	Wassermann Positive	Noguchi Positive
Primary syphilis	208	88 per cent	94 per cent
Secondary syphilis	669	92 per cent	98 per cent
Tertiary syphilis	455	74 per cent	83 per cent
Latent syphilis	305	54 per cent	68 per cent
Congenital syphilis	79	98 per cent	98 per cent
Cerebrospinal syphilis	55	73 per cent	80 per cent

Grading the Positive Reactions.—By making the *double sets* of experiments (Citron; Noguchi), one set (A) containing the amount of patient's serum and antigen given above, and the second set (B) containing half as much serum and half as much antigen, a rough quantitative report can be made, since the degree of inhibition of hemolysis varies according to the amount of syphilitic antibody present.

In Tube A, Noguchi uses 0.1 c.c. of aqueous extract antigen plus 0.1 c.c. of acetone-insoluble antigen; in Tube B only the acetone-insoluble antigen (0.1 c.c.).

If the serum be rich in syphilitic antibody, complete inhibition will occur in B as well as in A; such a reaction is marked "quadruple plus" (+ + + +). When the inhibition is incomplete in B but complete in A, the reaction is designated "triple plus" (+ + +). When hemolysis is complete in B, and inhibition complete in A, the reaction is said to be "double plus" (+ +). If there be only partial inhibition in A, and complete hemolysis in B, it is said to be "single plus (+). (See Plate II.)

Tube A	Tube B Half Quantities of Suspected Serum and of Antigen	Grade of Reaction
Complete inhibition	Complete inhibition	+ + + +
Complete inhibition	Partial inhibition	+ + +
Complete inhibition	Complete hemolysis	+ +
Partial inhibition	Complete hemolysis	+

Clinical Value of the Wassermann Reaction.—This reaction is of the greatest importance for the diagnosis of syphilis, and for the control of therapy in syphilis. During the past few years, in the clinic in which I work, between 50 and 100 Wassermann tests have been made per week (P. W. Clough; C. R. Austrian; W. A. Baetjer; R. W. Major; T. P. Sprunt; S. R. Miller; A. L. Bloomfield), and we have come to place great reliance upon results obtained when the technic outlined above is strictly followed.

A well-marked positive reaction is pathognomonic of syphilis (provided the patient is not suffering from scarlet fever, sleeping sickness, leprosy, or frambesia). Slight reactions are not to be regarded as positive; other tests should be done later. According to J. H. Richards (1913), the Wassermann reaction is often positive in diabetic acidosis in the absence of any luetic infection.

Single negative reactions do not rule out lues. The reaction may be negative in the blood and positive in the cerebrospinal fluid.

A serum that yields a negative reaction may become positive after a few doses of mercury, or after a single small salvarsan injection (*provocative stimulation*).

After prolonged treatment with mercury, iodids, or salvarsan, a serum formerly positive may become negative, and later on, after treatment has been stopped for some time, it may become positive again. At least 3 weeks should elapse after antiluetic treatment before making the test.

It is a safe rule to insist upon negative reactions, at intervals of 3 months, for at least 1 year after treatment has ceased before the patient can be pronounced free from infection. According to Craig and Nichols, the use of alcohol can exert a profound effect upon the results of a Wassermann test; it is asserted that through alcohol, a positive test can be converted into a negative one within 24 hours. Hough finds in dementia paralytica that alcohol has some influence, though not so great as in Craig's experience.

In *primary lues,* all cases examined are positive at the end of the fourth week after the appearance of the chancre (Swift); in 1 case, a positive Wassermann reaction was found 8 days after exposure and 14 days before the initial lesion appeared (Lesser). Probably 65 to 95 per cent of all primary cases will yield a positive Wassermann reaction. In *secondary lues,* the Wassermann reaction is positive in 75 to 95 per cent of the cases; in *hereditary lues,* in 90 to 100 per cent. In *cerebrospinal lues* about 90 per cent of the patients have a positive reaction in the blood serum (Naegeli).

Nearly all *general paretics* yield a positive reaction in both the blood (80 to 100 per cent) and the cerebrospinal fluid (73 to 100 per cent), while 50 to 75 per cent of *tabetics* yield a positive reaction in either the blood or the cerebrospinal fluid.

In the following table, taken from Noguchi's excellent monograph, the results of many observers in the different forms of lues are summarized.

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(From Noguchi, 3 Ed., pp. 110 and 111)

Investigators	Primary Syphilis		Secondary Syphilis Manifest		Tertiary Syphilis Manifest		Early Latent Syphilis		Late Latent Syphilis		Hereditary Syphilis		Cerebro-spinal Syphilis		General Paralysis		Tabes	
	No. Cases	% +	No. Cases	% +	No. Cases	% +	No. Cases	% +	No. Cases	% +	No. Cases	% +	No. Cases	% +	No. Cases	% +	No. Cases	% +
Wassermann, Neisser, Bruck, Schucht	25	91	101	73.3	37	78.4	41	85.4	53	88.7	...	...	...	...	...	...	...	...
Citron and Blaschko	64	90	56	98	23	91	67	80	51	57	...	...	10	60	...	...	...	...
Bruck and Stern	27	48.2	163	79.1	47	57.4	50	20	79	20	...	...	...	...	...	...	...	...
Bruhns and Halberstädter	9	88.9	50	98	16	100	39	43.3	82	28	...	...	...	...	...	...	...	...
Ledermann	19	52.6	56	100	27	92	41	75.6	19	36.8	16	100	26	88.5	23	87	68	76.4
Ledermann	46	61.2	110	98.1	78	96.2	115	83.8	78	53.8	...	...	...	...	...	...	...	...
Lesser	56	69	204	91	131	90	118	67	425	46	...	...	...	...	62	100	61	56
Noguchi	33	66.6	120	86.6	91	72.5	81	48.1	74	44.7	...	...	...	...	...	...	...	...
Hoehne	44	38.6	329	79.1	33	63.6	387	31.3	...	...	24	87.5	12	16.7	30	80	45	60
Boas	50	60	395	100	63	97	294	47	...	...	...	...	...	...	42	100	20	80
Detre and Brezovsky	43	98	21	81	35	73	...	...	...	...	...	...	...	...	...	...	...	...
Boas and Thomsen	...	...	...	...	...	...	...	...	...	...	32	87.5	...	...	...	...	...	...
Bauer	...	...	...	...	...	...	...	...	...	...	22	100	...	...	...	...	...	...
Halberstädter, Müller and Reiche	...	...	...	...	...	...	...	...	...	...	27	92	...	...	...	...	...	...
Noguchi	...	...	...	...	...	...	...	...	...	...	4	100	2	50	...	...	22	40.9
Nonne	...	...	...	...	...	...	...	...	...	...	...	...	...	(20)	...	(90)	...	(90)
Frenkel-Heiden	...	...	...	...	...	...	...	...	...	...	...	...	7	27	14	78.5	...	...
Plaut	...	...	...	...	...	...	...	...	...	...	...	...	4	25	180	100	...	...
Stertz	...	...	...	...	...	...	...	...	...	...	...	...	3	66	45	95.5	...	...
Marie, Levaditi, Yamanouchi	...	...	...	...	...	...	...	...	...	...	...	...	...	...	30	59	...	...
Raviart, Breton and Petit	...	...	...	...	...	...	...	...	...	...	...	...	...	...	72	93	...	...
	416	69.8	1605	89.4	581	78.1	1233	51	861	47	125	94.5	64	47.6	498	88.1	216	62.66

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ii. Complement-Fixation Test for Differentiation of Human from Animal Blood (Gengou-Moreschi Phenomenon)

Here, use is made of complement-fixation for forensic purposes (Neisser and Sachs). It has the same value as the precipitin test (q. v.) but is more difficult to carry out, and, though more sensitive, is less specific. For the technic, the original articles may be consulted.

iii. Complement-Fixation in the Diagnosis of Echinococcus

The serum of patients suffering from echinococcus invasion can be recognized by the use of the complement-fixation test in which the unaltered hydatid fluid of infected sheep is used as antigen. Or an antigen may be made by extracting the walls of echinococcus cysts with water or with alcohol. The reaction was positive in 10 out of 12 cases examined by Thomsen and Magnussen. According to Meyer and Hahn, it is a group reaction, the test being positive with different forms of tenia.

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iv. Complement-Fixation in the Diagnosis of Gonococcal Infections

This method, applied first by Mueller and Oppenheim (1906) has been used in this country especially by Schwartz and McNeil, O'Neil, Kyes, and

Keidel and seems to be valuable in the diagnosis of chronic gonococcal infections (gonococcus arthritis, etc.).

Cultures of the gonococcus on salt-free veal agar, neutral to phenolphthalein, are used as antigen; it is best to have cultures from at least a dozen strains, and to mix them. For details of preparation of the antigen, see the article of Schwartz and McNeil. The gonococcus antigen sold by Parke, Davis & Co. is said to work well.

Technic.—The *hemolytic amboceptor is titrated* in the ordinary way. In a series of hemolyzing tubes is placed 0.5 c.c. of complement (1:10). Each of the tubes then receives varying amounts of antisheep rabbit serum, and the total quantity in each tube is then brought up to 1.5 c.c. with physiological salt solution. With a pipet, 0.5 c.c. of washed sheep's corpuscles (5 per cent suspension) is next added to each tube, so that the total volume in each tube is now 2 c.c. The rack of tubes is then placed in the thermostat at 37° C. for 1 hour, at the end of which time one notes the smallest amount of hemolytic amboceptor that has caused complete hemolysis. This amount is designated *1 unit* of hemolytic amboceptor; in subsequent tests, 2 units are used.

In *titrating the antigen,* a rack containing a double row of tubes is used. Into each tube of the back row is placed 0.1 c.c. of normal human serum from a person certainly free from gonococcal infection, while into each tube in the front row is placed the same amount of human serum from a patient suffering certainly from gonorrhea and known to have a serum strongly positive. If such a serum be not available, the same amount of antigonococcic serum, prepared for therapeutic purposes, may be used in its place. Increasing quantities of gonococcus antigen are now introduced into each consecutive pair of front and back tubes, and the quantity of fluid in each tube brought up to exactly 1 c.c., after which 0.5 c.c. of complement (1 part of guinea-pig's serum + 9 parts physiological salt solution) is added. The rack of tubes is then placed in the thermostat at 37° C. for 1 hour, after which 0.5 c.c. of sheep's corpuscles (5 per cent suspension) and 2 units of hemolytic amboceptor are added to each tube. The rack of tubes is then replaced in the thermostat for another hour, after which the tubes are examined; the smallest amount of antigen that has caused complete inhibition of hemolysis with the gonorrheal serum but which has not interfered with hemolysis with the normal serum is called the *unit of antigen.* Two units of antigen are used in subsequent tests. Therefore one should observe whether two units of antigen show any tendency to inhibit hemolysis in the series with normal serum. If so, the antigen should be discarded, and a fresh antigen prepared.

The Actual Test.—After both hemolytic amboceptor and antigen have been titrated, the 12 test tubes are arranged in a rack as in the following diagram:

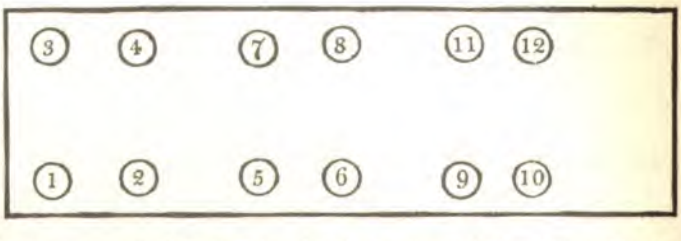

Fig. 53.—Arrangement of Test Tubes for the Gonococcal Complement-Fixation Test. (After G. F. Dick.)

The contents of the tubes are as follows:

TABLE SHOWING ARRANGEMENT OF TUBES FOR COMPLEMENT-FIXATION TEST IN GONOCOCCAL INFECTIONS

Tube Number	Patient's Serum c.c.	Normal Serum c.c.	Positive Serum c.c.	Antigen Units
1	0.05	0	0	2
2	0.1	0	0	2
3	0.05	0	0	0
4	0.1	0	0	0
5	0	0.05	0	2
6	0	0.1	0	2
7	0	0.05	0	0
8	0	0.1	0	0
9	0	0	0.05	2
10	0	0	0.1	2
11	0	0	0.05	0
12	0	0	0.1	0

Enough physiological salt solution is added to make the contents of each tube measure 1.5 c.c. The whole rack is then placed in the thermostat at 37° C. for 1 hour.

To each tube the secondary hemolytic system is now added, that is, in each tube is placed 2 units of hemolytic amboceptor and 0.5 c.c. of sheep's corpuscles (5 per cent suspension), and the rack of tubes replaced in the thermostat for another hour.

The tubes are then examined. If the *reaction be positive,* Tubes 1 and 2 and Tubes 9 and 10 should show no hemolysis; in all the other tubes, the corpuscles should be completely hemolyzed. If preferred, Noguchi's human system can be used instead of the sheep system, just as with the Wassermann test.

Results of the Gonococcus Complement-Fixation Test.—The reaction is rarely positive before the fourth week of the disease, and then only in acute cases with complicating prostatitis or arthritis. Once present, the reaction usually persists for a couple of months; should it be present still longer, it indicates the persistence of the infection.

The test is usually negative in uncomplicated *acute anterior urethritis,* but here smears yield the positive diagnosis.

In chronic posterior urethritis, prostatitis, vesiculitis and gonorrheal stricture, 5/6 of the cases yield a positive reaction (O'Neil).

In females, the majority of cases of infection of the lower genital tract yield a positive reaction.

In pelvic infections, the reaction is also usually positive, especially if the cervix uteri be involved.

In gonorrheal arthritis, the reaction is usually positive.

In vulvovaginitis in children, the reaction is positive (McNeil).

The test differs from the Wassermann reaction in that it is biologically specific, depending upon a specific antigen-antibody interaction. Accordingly, non-gonorrheal cases never yield a positive reaction (Schwartz and McNeil).

The test requires, as Irons emphasizes, a considerable degree of skill for its performance, and adequate controls are essential. It is important to remember that a negative result does not exclude gonococcal infection.

In cases of gonococcal arthritis, the reaction may vary from positive to negative within a few days, but if in a case of arthritis the reaction is persistently negative when repeated at intervals of 4 to 7 days, it is strong evidence against a gonococcal origin.

In our clinic, and in Young's urological clinic, this test, by Keidel, has been of considerable help in differential diagnosis.

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3. Tests for Precipitins

Clinically, the precipitin tests are useful as biological blood tests in medico-legal cases (Uhlenhuth).

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(*a*) *Precipitin Test for Human Blood*

The suspected material is dissolved in salt solution and diluted so that 1 c.c., on boiling with a drop of 25 per cent HNO_3, shows only a slight opalescence.

Six small tubes are placed in a rack. In tubes I and II are placed 1 c.c. of the solution of the suspected material, in Tubes III and IV, 1 c.c. of diluted cat's or dog's blood, in Tube V, 1 c.c. of salt solution, and in Tube VI, 1 c.c. of a 1:1000 solution of human blood. Next, 0.1 c.c. of serum from a rabbit immunized against human blood is added to each of the tubes except Tube II, which receives 0.1 c.c. of normal rabbit's serum. The serum added is allowed to flow down the side of each tube. The tubes are left at the room temperature, without shaking, for 20 minutes, and then examined. If the suspected material is human blood, a precipitate will be seen in Tubes I and VI, while Tubes II, III, IV and V will remain clear.

The test is very sensitive; dried blood-stains 50 years old, or older, are recognizable.

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(*b*) *Precipitin Test for Meningococcal Infection*

Vincent and Bellot have devised a diagnostic test for epidemic cerebrospinal meningitis dependent upon a precipitin reaction. They add 1 drop of antimeningococcus serum to 3-6 c.c. of cerebrospinal fluid (cleared by centrifugation), and allow to stand for 8-12 hours at 50°-53° C. A precipitate, it is asserted, indicates a meningococcic infection, even in the absence of meningococci from smears and cultures.

4. Tests for Immune Opsonins (Bacteriotropins)

Technic.—Leukocytes, serum and bacteria in definite proportions are mixed in a test tube Phagocytosis occurs, the leukocytes engulfing the bacteria. Stained preparations are made and 100 leukocytes counted, as well as the number of bacteria visible within them. The average number per leukocyte is called the *phagocytic count,* while the number obtained by dividing this by the phagocytic count as obtained in a normal person is called the *opsonic index;* thus, if the average number of organisms per cell is 5 when the patient's serum is used and is 10 when normal serum is used, the opsonic index of the patient for the particular bacterium used will be 0.5. According to Wright and Bulloch, the opsonic index in normal persons varies between 0.8 and 1.2.

The technic is difficult and time-consuming and only laboratory men working constantly with it can obtain reliable results. The diagnostic value is much disputed.

In our clinic, we gave the methods a fair trial (Cole and others) and have abandoned them as far as practical clinical work is concerned. When variations in index beyond the limits of error occur, other changes, easier to recognize, will permit of a diagnosis. The details of the technic can be found in Wright's articles, and also in C. E. Simon's Infection and Immunity.

5. Tests for Ergins

When the human body is in an allergic, or anaphylactic, state, inoculation with the corresponding antigen (or allergin) calls forth a specific reaction, probably due to union of the allergin with certain specific antibodies (ergins).

Certain clinical allergic tests are much in use; notably (1) the tuberculin tests, (2) the luetin test, (3) Austrian's ophthalmo-reaction in typhoid, and (4) Pfeiffer's anaphylactic protein test.

(*a*) *Tuberculin Tests*

i. Subcutaneous Tuberculin Reaction (Koch)

When old tuberculin (Koch) is injected, subcutaneously, into healthy people, considerable quantities can be borne without any symptoms, while tuberculous patients react to very small doses (0.1–1 mg.) with outspoken symptoms.

Three forms of reaction are distinguished: (1) a general reaction, (2) a focal reaction, and (3) a puncture or local reaction.

General Reaction.—Fever, malaise, headache, pains in the limbs, palpitation, nausea and vomiting. The most important symptom is the rise of temperature.

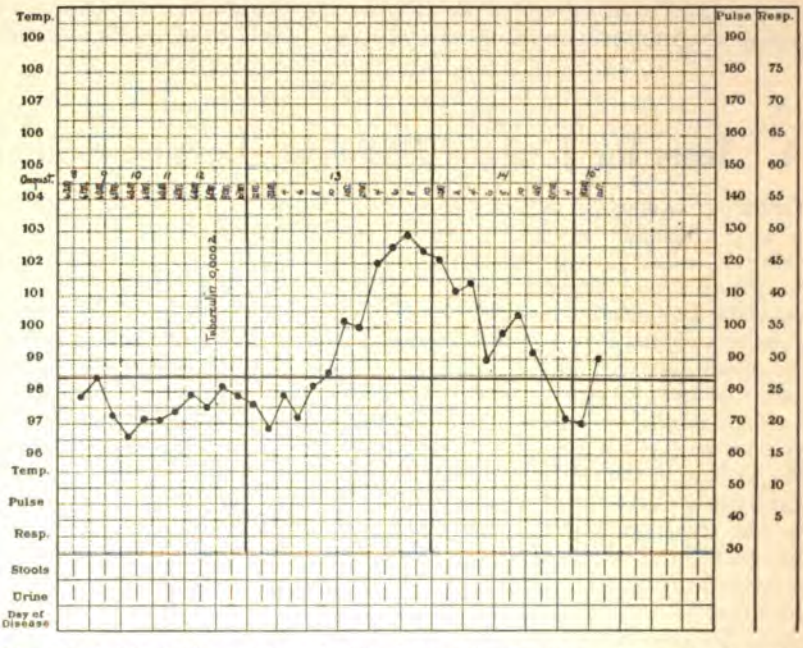

Fig. 54.—Chart Illustrating a Characteristic Tuberculin Reaction. (From L. Hamman and S. Wolman.)

Focal Reaction.—Evidences of irritation in the diseased tissue; thus, in *pulmonary tuberculosis,* increased râles, cough, and sputum; or, in *tuberculosis of the skin, eye* or *larynx,* a visible flare-up of the inflammatory process.

Puncture Reaction, or Local Reaction.—Redness and swelling and pain at the site of the aseptic injection. The regional lymph glands are often swollen and tender.

In making this test, the patient should be afebrile, and the temperature should be recorded every 2 hours during the 48 hours preceding. On the third day, the dose

is administered subcutaneously, preferably in the back (between the scapulæ). It is best to give 1/5 mg. as the initial dose, 1 mg. as the second, and 5 mg. as the end dose in adults (Hamman and Wolman), at intervals of 3 days when more than one dose is required. A rise of temperature to 100° F., or higher, is regarded as a positive reaction. As a diluent of the tuberculin, 0.8 per cent salt solution, containing 0.25 per cent carbolic acid, is used.

If there be no reaction after three injections given as above, it can be assumed that the patient is free from active tuberculosis. The test is contra-indicated after hemoptysis or hematuria. Careful physical examinations of the patient should be made just before each injection is given and the results closely compared with the findings after the test.

ii. Cutaneous Tuberculin Reaction (von Pirquet)

This is especially useful for the diagnosis of tuberculosis in young children.

Technic.—Cleanse the skin of the flexor surface of the forearm with alcohol or ether; apply a small drop of old tuberculin at each of two points about 10 cm. apart. With von Pirquet's "borer," or with a needle, or the point of a scalpel, make a superficial abrasion, first in the skin midway between the two drops, and then in the center of each drop of tuberculin. It is best to avoid free bleeding; it is enough to scarify so that a few small points of blood appear. Leave exposed to the air for 5 to 10 minutes; this insures the maximum amount of absorption. Then gently wipe with absorbent cotton, avoiding the control point. No dressing is required.

After 24 hours the inoculated points are carefully compared with

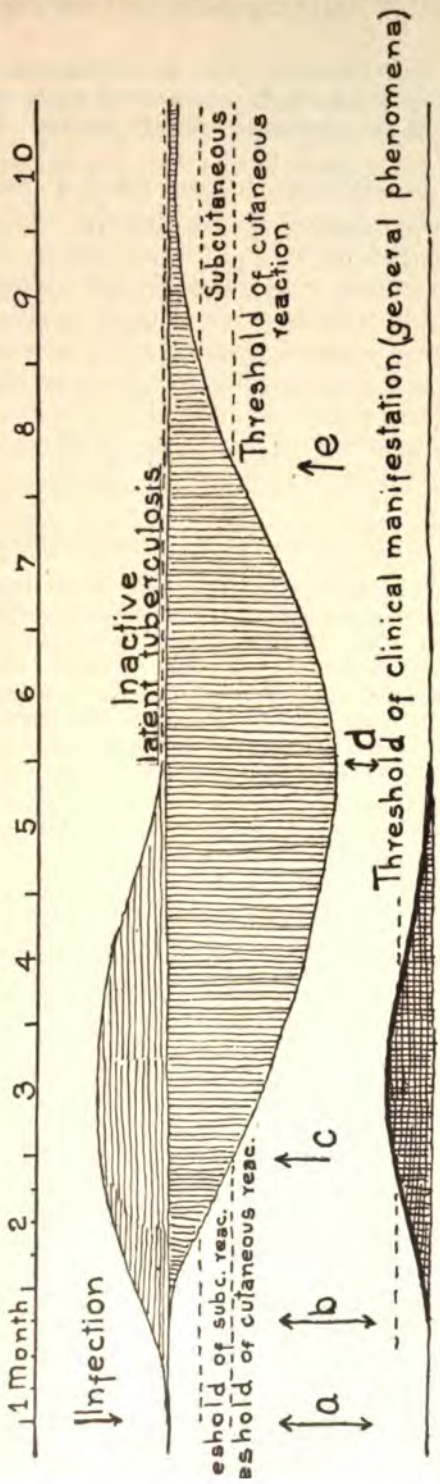

Fig. 55.—Course of Benign Infection of Man with Tuberculosis. (After C. E. von Pirquet, Arch. Int. Med.)

the control between them. If the borer has been used, the control shows a traumatic reaction; if the inflammatory areola be 5 millimeters or more wider than the control, the reaction is definitely positive. (See Plate III, Fig. 4.)

In scrofulous children, the skin about the area of reaction may show a number of small elevated nodules, and similar nodules may appear at the same time upon the limbs and trunk. The reaction is specific. Tuberculous patients react unless the tuberculosis be (1) very acute (general miliary tuberculosis, tuberculous meningitis, galloping phthisis), (2) the end-stage of a chronic process, or (3) associated with other acute infections.

For diagnostic purposes, the reaction is very valuable in schools, and in children under two years of age; in older children and in adults, it is positive in more than 70 per cent of all examined, and is, therefore, of no diagnostic value in them.

Other Tuberculin Reactions Applied to the Skin

These include (a) the *percutaneous tuberculin test* (Moro), in which 50 per cent tuberculin-lanolin is rubbed into the skin for 1 minute, and (b) the *intracutaneous tuberculin test* (Mendel-Mantoux), in which a dilute solution of old tuberculin is injected *into* the skin through a fine needle, as in the Schleich method of local anesthesia. The information furnished by this test is intermediate in value between that given by the conjunctival and the cutaneous tests.

The so-called *differential cutaneous reaction* of Detre, intended to decide between human and bovine tuberculosis, is of doubtful value.

Attempts at *quantitative tuberculin tests* for determining the degree of sensitiveness have been made by White and Graham, by White and Van Norman, and by Boardman.

iii. Conjunctival Tuberculin Test or Ophthalmo-Reaction (Calmette; Wolff-Eisner)

In this test, a salt-solution dilution of tuberculin is instilled into the conjunctival sac. The appearance of a conjunctivitis in 12 to 24 hours is the criterion of a positive reaction.

Technic.—Freshly prepared sterile dilutions (1:100; 5:100) of old tuberculin (Höchst) in normal salt solution are used. The eyes are inspected to exclude disease and to make sure that the conjunctivae of the two sides correspond in appearance. The lower lid is drawn forward while the patient looks lateralward, and 1 drop of the weaker solution is placed at the medial canthus with an eye-dropper (or, better, with Baldwin's capillary pipet), avoiding lacrimation. Examine at the end of 24 hours.

Three groups of positive reactions are distinguished:

1. *Mild reaction:* Redness at the medial canthus (caruncle), and on the inner surface of the lower lid.

2. *Medium reaction:* The same, plus involvement of the conjunctiva bulbi.

3. *Violent reaction:* Purulent conjunctivitis, rarely with vesicles.

If the reaction be negative, a drop of the 5 per cent solution may be placed in the other eye. If it yield a positive reaction, not much stress is laid upon it, but if it yield a negative reaction, this speaks strongly against active tuberculosis.

Precautions.—The conjunctival test should never be repeated in the same eye for fear of overwhelmingly severe reaction, due to local sensitization. The test should not be made if the eye be in any way diseased, or if the adjacent skin be affected. It is also best avoided in manifestly scrofulous children and in aged persons. If these precautions be observed, one may, in my experience, use the ophthalmic test without fear of untoward symptoms.

Value of the Ophthalmo-Reaction.—I lay great stress upon a positive reaction with 1 per cent solution as indication of the presence of "clinical" tuberculosis. A negative result with 1 per cent solution is of but little value, but a negative result with 5 per cent solution is of real value in helping to exclude clinical tuberculosis.

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(b) *Epiphanin Reaction (Weichardt)*

The presence of either antigen, or of antibodies, in minute traces can be demonstrated by the epiphanin reaction (Weichardt), which depends upon the acceleration of diffusion when antigen and antibodies are brought together in certain dilutions.

The test can be made with Weichardt's diffusiometer (Zentralbl. f. d. gesamte Phys. u. Path. d. Stoffwechsels, 1911, Nr. 9). It has been made more delicate by introducing a second system ($Ba(OH)_2$ and H_2SO_4) and noticing whether there is a dislocation of the end-reaction with phenolphthalein as indicator, as contrasted with controls, through the antigen-antibody union. We probably have to deal here with absorption changes of a changing colloid (Schade).

The simpler modification of the test suggested by v. Angerer and Stötter (1912) is the one now generally used.

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(c) *Meiostagmin Reaction (Ascoli)*

This reaction depends on the principle that, on adding antigen to diluted serum, changes occurring in a colloid system can be recognized by changes in the surface-tension of the fluid. In case the antigen unites with antibodies in the serum, the surface-tension is diminished. This can be measured by dropping the serum from a small tube (Traube's stalagmometer). The drops become smaller and their number greater.

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(d) *Potassium-Iodid-Starch Method for Measuring the Excitation of Catalyser Action by Proteotoxic Substances (Weichardt and Kelber)*

Cleavage products of proteins and other toxic substances can influence catalysers such as hemoglobin and colloidal metals (e. g., colloidal osmium) in a characteristic

way. This influence on the catalyser can be measured quantitatively by the method of Weichardt and Kelber. (See original article, Münch. med. Wchnschr., 1912, Nr. 35.)

These tests may be valuable for investigative work, but as yet are not clinically applicable.

(*e*) *Luetin Test* (*Noguchi*)

This is a cutaneous reaction for syphilis similar to the intracutaneous test for tuberculosis. The luetin is injected with a fine needle just beneath the epidermis, the needle being advanced for a short distance. The devising of the test became possible after Noguchi grew *Treponema pallidum* in pure culture.

Technic.—Luetin consists of killed cultures of *Treponema pallidum* in thin emulsion. As a control fluid, a preparation made from the sterile culture medium is employed. The arms are sterilized with alcoholic sublimate solution. The left arm is injected intradermally with 0.07-0.10 c.c. of luetin at two points 5 cm. apart. The right arm is similarly injected with the control fluid. In non-syphilitic individuals, the reactions (traumatic) are identical in the two arms, appearing as a small rosy areola, with or without slight swelling, from 24 to 48 hours after injection, and disappearing within 48 hours without induration. In syphilitic patients, the reactions may differ markedly on the two sides. At the site of the luetin injection a large reddish, indurated papule may appear in 24 to 48 hours, about 7 to 10 mm. in diameter; it increases in size and becomes surrounded by a red zone **(papular reaction)**. It may require 4 to 5 days for evolution and then gradually undergo involution, turning bluish red, then fading, to disappear entirely in about 2 weeks. Or, it may, about the fourth day, become vesicular, and a day or two later purulent **(pustular reaction)**. In this case, the pustule usually ruptures, and a crust forms; after the crust falls off, an indurated nodule remains for weeks or months. This pustular type of reaction is common in late hereditary syphilis, in tertiary lues, and in secondary lues after treatment with salvarsan.

In rare instances, the reaction seems to be negative at first, but after 10 days, or later, the inoculated points become markedly inflamed, sometimes with pustule formation **(torpid form of reaction)**.

Value of the Reaction.—The Noguchi luetin test seems to be especially serviceable in the recognition of (1) congenital lues, (2) latent syphilis, and (3) the late stages of lues in adults. The method has been carefully controlled in the clinic in which I work by Wolfsohn (1912), who found that, in tabes and in dementia paralytica, the reaction may be delayed for from 9 to 30 days. A reaction sometimes occurs at the control site, especially in tertiary lues. The luetin test is a good supplement to the Wassermann reaction since it often yields positive reactions in the luetic conditions in which the Wassermann reaction is occasionally negative.

Long continued treatment, still short of cure, tends to render the luetin reaction more evident; while it makes the Wassermann reaction negative.

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(*f*) *Typhoprotein Conjunctival Test, or Typhoid-Ophthalmo-Reaction (Chantemesse; Austrian)*

The method is of value, especially if the antigen be prepared by Austrian's method (10 mg. of dry bacillary protein added to 1 c.c. distilled water).

Technic.—One drop of a solution of the dry bacillary protein (0.0005 gram) is instilled into the conjunctival sac after slightly everting the lower lid, and the eye examined, at short intervals, during the first 24 hours. Two kinds of reaction are met with: (a) the typical diagnostic reaction and (b) the atypical non-diagnostic reaction.

Typical or Diagnostic Reaction.—This appears in 1 to 5 hours after instillation, and is usually maximal within 6 to 10 hours (injection of vessels of conjunctiva of lower lid, reddened or purplish caruncle, slight edema of lid, drop of pus). Usually the conjunctiva of the lower lid shows a bright purple color and looks velvety. There is slow subsidence after 10 to 20 hours. It may require 10 days for complete subsidence. There is no pain or photophobia. The congestion persists for at least 24 hours.

Atypical, Non-Diagnostic Reaction.—Normal persons, and patients other than typhoids, may show an atypical or non-specific reaction (greater injection of conjunctiva bulbi, more pus); less reaction in palpebral conjunctiva and caruncle, fading rapidly in 4 to 14 hours.

Value of Reaction.—When typical, it agrees closely with the results of blood cultures, helping to establish the diagnosis earlier in the disease than the Widal reaction.

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(g) *Anaphylactic Test for Protein (Pfeiffer)*

For forensic purposes, the anaphylactic phenomenon in the guinea-pig, as shown either by death in convulsions from anaphylactic shock, or by a sudden fall of temperature or fever, with fall of blood-pressure and later eosinophilia may be utilized for testing a suspected protein. A guinea-pig is injected with 0.1 c.c. of blood serum, or with a small amount of protein of known origin. After 14 to 21 days, 1.0 to 2.0 c.c. of a solution of protein, suspected to be the same as that by which the animal has been sensitized, is injected. If the suspicion be correct, the guinea-pig will show a marked fall in temperature and will probably die in acute anaphylactic shock. This method can be employed instead of the precipitin method, especially if the material has undergone marked change. Brück has used the *method of passive anaphylaxis* to demonstrate idiosyncrasy to antipyrin.

SECTION II

SPECIAL DIAGNOSIS OF THE INFECTIOUS DISEASES

A bird's-eye view of the principal infectious diseases and the etiological agents concerned in them can be obtained by a study of the following tables.

ETIOLOGICAL AGENTS IN THE PRINCIPAL INFECTIOUS DISEASES

I. VEGETABLE MICROÖRGANISMS

(*a*) *Cocci as Infectious Agents*

i. *Streptococcus:* Erysipelas; anginas; phlegmons; septicemias; peritonitis; endocarditis acuta; endocarditis lenta; bronchopneumonia; acute rheumatic fever.
ii. *Staphylococcus:* Furunculosis; septicemias, and especially pyemia; endocarditis; osteomyelitis.
iii. *Pneumococcus:* Croupous pneumonia; otitis; meningitis; peritonitis; endocarditis; arthritis; pericarditis; empyema.
iv. *Gonococcus:* Urethritis; prostatitis; epididymitis; orchitis; pyelitis; vulvovaginitis; pelvic peritonitis; salpingitis; endometritis; endocarditis; polyarthritis; ophthalmia neonatorum.
v. *Meningococcus:* Epidemic cerebrospinal meningitis; polyarthritis.
vi. *Micrococcus mellitensis:* Malta fever.

(*b*) *Bacilli as Infectious Agents*

i. *Pneumobacillus* (Friedländer): Pneumonia; serositis; meningiti
ii. *Scleroma Bacillus:* Rhinoscleroma.
iii. *Bacillus anthracis:* Anthrax.
iv. *Bacillus edemæ malignæ:* Malignant edema.
v. *Bacillus aerogenes capsulatus* (Welch and Nuttall): Gas gangren
vi. *Bacillus tetani:* Tetanus.
vii. *Bacillus influenzæ:* Influenza (nasopharyngitis; paranasal sin sitis; bronchitis; bronchopneumonia; meningitis; encephaliti endocarditis, etc.).
viii. *Bacillus of Bordet and Gengou:* Whooping-cough.
ix. *Bacillus pestis:* Bubonic plague (bubo; sepsis; pneumoni
x. *Bacillus typhosus:* Typhoid fever.

xi. *Bacillus paratyphosus* A and B and Manchuriensis: Paratyphoid fever.
xii. *Bacillus coli communis:* Peritonitis; cholangitis; pyelitis; cystitis.
xiii. *Bacillus dysenteriæ* (Shiga; Flexner): Bacillary dysentery.
xiv. *Bacillus of Ducrey:* Soft chancre (ulcus molle).
xv. *Bacillus diphtheriæ* (*Loeffler*): Diphtheria (throat; nose; larynx).
xvi. *Bacillus pyocyaneus:* Green pus; various inflammations.
xvii. *Bacillus mallei:* Glanders (skin; lymphatics; lungs, etc.).
xviii. *Bacillus tuberculosis* (Koch): Tuberculosis (general miliary; pulmonary; meningeal; serosal; articular; cutaneous; urogenital, etc.).
xix. *Bacillus lepræ:* Leprosy.
xx. *Bacillus choleræ asiaticæ* (Koch): Asiatic cholera.
xxi. *Bacillus lacti morbi:* Milk sickness.
xxii. *Bacillus proteus vulgaris:* Acute infectious jaundice (epidemic catarrhal jaundice; Weil's disease).
xxiii. *Bacillus typhi-exanthematici:* Typhus fever.

(*c*) *Coarser Forms of Fungi as Infectious Agents*

i. *Hyphomycetes:*
  (a) *Aspergillus:* Aspergillosis (lungs; skin; ear; nose; cornea).
  (b) *Mucor:* Mucor-mycosis (lung; ear; intestine).
  (c) *Achorion:* Favus (skin; sepsis).
  (d) *Tricophyton:* Ringworm.
  (e) *Microsporon furfur:* Pityriasis versicolor.
  (f) *Microsporon minutissimum:* Erythrasma.
ii. *Blastomycetes:*
  (a) *Blastomyces* and *Oidium:* Dermatitis; metastatic granuloma.
  (b) *Thrush fungi:* Thrush (parasitic stomatitis).
iii. *Sporotrichum* or *Sporothrix:* The Sporotrichoses.
iv. *Streptothrix* (The Streptotrichoses):
  (a) *Streptothrix actinomyces:* Actinomycosis (head; neck; lungs; intestines; bones).
  (b) *Mycetoma fungi:* Madura foot.
  (c) *Other Streptothrix forms:* The pseudo-actinomycoses.
  (d) *Discomyces:* The Gougerot-Carougeau nocardiosis.

II. Animal Microörganisms (Protozoa)

(*a*) *Rhizopoda as Infectious Agents*

i. *Entameba histolytica:*
  Amebic dysentery.
  pical liver abscess.
  a alveolaris.

(*b*) *Mastigophora as Infectious Agents*

i. *Trypanosomidæ:*
   (a) *Trypanosoma gambiense:* Sleeping sickness; trypanosome fever.
   (b) *Typanosoma rhodesiense:* Kaodzera.
   (c) *Schizotrypanum cruzi:* Chagas' disease.
ii. *Piroplasmidæ:*
   (a) *Leishmania* (*donovani*): Kala-Azar.
   (b) *Leishmania* (*infantum*): Infantile Kala-Azar.
   (c) *Leishmania* (*tropica*): *Oriental sore* (Delhi boil).
iii. *Plasmodidæ:*
   (a) *Plasmodium vivax:* Tertian malaria.
   (b) *Plasmodium malariæ* (Laveran); Quartan malaria.
   (c) *Plasmodium immaculatum* (*sive præcox*) (Grassi and Feletti): Estivo-autumnal malaria.
iv. *Spirochæta obermeieri, duttoni, novyi, carteri:* Relapsing fever.
v. *Treponema pallidum* (*Spirochæta pallida*): Syphilis and parasyphilis.
vi. *Treponema pertenu:* Yaws or frambesia.
vii. *Treponema pallidum:* Granuloma venereum.
viii. *Gangosa.*
ix. *Verruga peruana.*
x. *Bartonia bacilliformis:* Oroya fever.

(*c*) *Sporozoa as Infectious Agents*

III. Filtrable Viruses (Ultramicroscopic)

(a) *Pasteur's Virus:* Rabies (hydrophobia; lyssa).
(b) *Reed, Carroll and Agramonte's Virus:* Yellow fever.
(c) *Ashburn and Craig's Virus:* Dengue fever.
(d) *Flexner and Noguchi's Virus:* Poliomyelitis (Heine-Medin disease).
(e) *Loeffler and Frosch's Virus:* Stomatitis epidemica (foot and mouth disease); *Doerr and Russ's Virus:* Pappataci fever; *Peyton Rous's Virus:* Sarcoma.

IV. Unknown Infectious Agents

(*a*) *The Acute Exanthemata*

i. Scarlet fever.
ii. Measles.
iii. Rubeola.
iv. Rubeola scarlatinosa (Fourth Disease).

v. Chickenpox (Varicella).
vi. Smallpox (Variola).
vii. Vaccinia (Cowpox and vaccination).
viii. Sweating Sickness (Febris miliaris).
ix. Rocky Mountain Spotted Fever.

(*b*) *Non-exanthematous Diseases*

i. Mumps (Parotitis epidemica).

I. DISEASES DUE TO VEGETABLE MICROÖRGANISMS

A. Diseases Due to Cocci

1. Diseases Due to Streptococci

The pathogenic streptococci, more often than any other bacteria, are the cause of septicemia. Over 60 per cent of general infections in which bacteria can be grown from the blood are due to streptococci. (Plate III, Figs. 2 and 3.)

These cocci grow in shorter or longer chains. They do not decolorize by Gram. They grow well on ordinary media, not liquefying gelatin.

Several varieties of streptococci are differentiable by cultivation on blood-agar plates, in which they show differences (1) in hemolysin formation and (2) in pigment production (Schottmüller).

1. **Streptococcus pyogenes** or **Streptococcus vulgaris hemolyticus.**—Each colony in the blood-agar plate is surrounded by a circular clear area, due to the absorption of hemoglobin (hemolysis).

2. **Streptococcus viridans.**—This grows more slowly on blood-agar plates, often not appearing for several days. The colonies develop as fine greenish points, in the depth usually smaller in size than the head of a pin. Those on the surface may be somewhat larger, and are blackish green or gray. There is no clear area of hemolysis about the colony. Milk is coagulated in from 1 to 3 days.

3. **Streptococcus putridus.**—Strictly anaërobic; does not cause hemolysis on blood-agar plates. Cultures have a foul odor (H_2S). Colony white. Does not coagulate milk. Non-pathogenic for animals.

4. **Streptococcus mucosus.**—Cocci in capsulelike hull. Aërobic, and facultative anaërobe. Milk coagulated in 24 to 48 hours. Colonies on blood-agar dark green; larger than head of a pin in 24 hours. Highly pathogenic for animals (white mice, rabbits).

Of the above four varieties, the first, or *Streptococcus hemolyticus,* is the most common cause of sepsis; *Streptococcus viridans* is the cause of

subacute infectious endocarditis (endocarditis lenta), while *Streptococ[illegible] putridus* is often the septic agent in infections following abortion.

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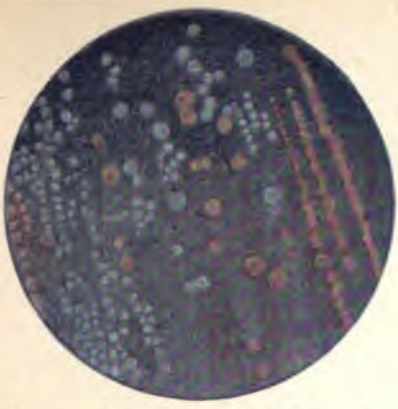
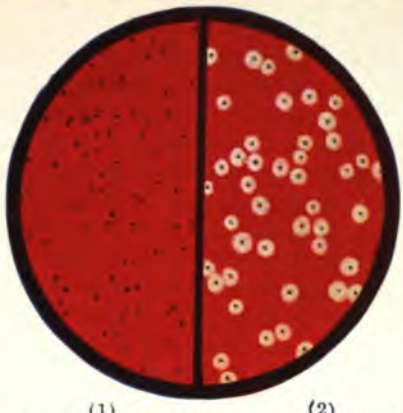


Fig. 1.—Conradi-Drigalski Plate. B. Typhosus—Blue Colonies. B. Coli—Red Colonies. (After L. Mohr u. R. Staehelin, "Handb. d. inner. Med.," published by J. Springer, Berlin.)



(1) (2)

Fig. 2.—Differentiation of Streptococci on Blood-agar Plate. (1) Streptococ. vulgar. haemolyticus, (2) Streptococcus mitior. (After G. Jochmann, in L. Mohr u. R. Staehelin, "Handb. d. inner. Med.," published by J. Springer, Berlin.)

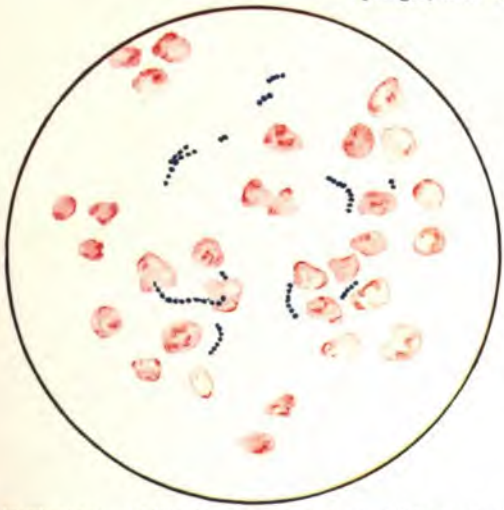


Fig. 3.—Pus with Streptococci. (After G. Jochmann, in L. Mohr u. R. Staehelin, "Handb. d. inner. Med.," published by J. Springer, Berlin.)

Fig. 4.—Quantitative Gradation of the Cutaneous Reaction After von Pirquet. (After P.

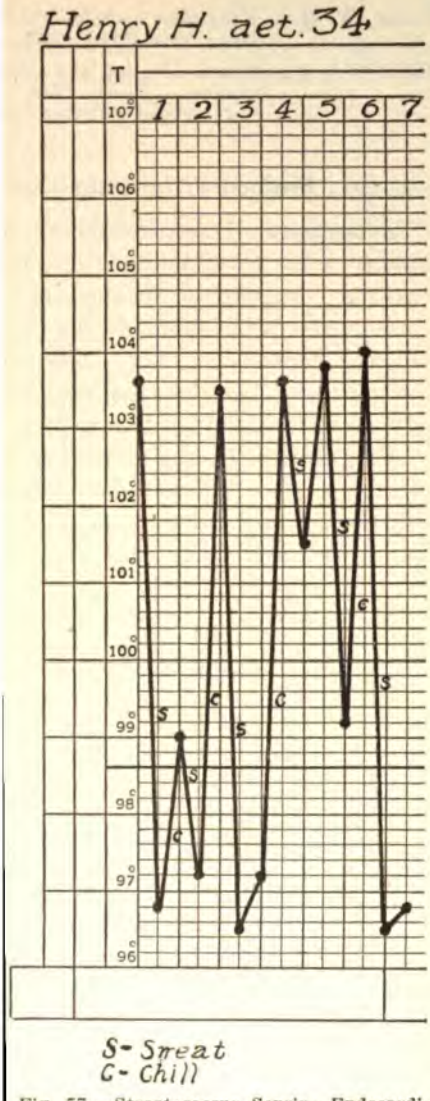


Fig. 57.—Streptococcus Sepsis; Endocarditis ulcerosa. (Personal Observation.)

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(*b*) *Endocarditis lenta* (*Subacute Infectious Endocarditis*)

Symptoms.—Onset insidious; slight fever at first, later high and intermittent with or without chills; gastro-intestinal disturbances common; sweating; progressive weakness and emaciation; signs of valvular disease usually present but often lacking; palpable spleen; pains in bones, joints, or muscles; tenderness over lower sternum; progressive anemia; painful erythematous nodules; sallow facies; pigmentation; petechiæ. The patients have nearly all had rheumatic endocarditis in earlier life.

Diagnosis.—This is usually easy if the blood culture is properly made (*Streptococcus viridans*). In the differential diagnosis, *rheumatic endocarditis, typhoid fever, malarial fever, tuberculosis,* and *Banti's disease,* should be considered. (See next page.)

For the Differentiation of the Endocarditis-Cocci, the Following Table is Useful (Austrian)

	Pneumococcus	Streptococcus	Cocci of Endocarditis lenta	
			A	B
Capsule	1. Diagnostic or 2. Not present	1. Non-diagnostic or 2. Not present	Not present	Not present
Gram	Positive	Positive	Positive	Positive
Blood-plates	Green, no clear zone	1. Gray, clear zone, or 2. Green, no clear zone, or 3. Moist white growth	1. Green, no clear zone or 2. Moist or dry white growth, no clear zone	
Inulin fermentation	+ (occasionally −)	− (rarely +)	+	−
Precipitation Serum, Glucose-Agar	− (rarely +)	+	+	+
Solution by Bile	+	−	−	−
Appearance in 1st culture	24–48 hrs.	24–48 hrs.	24–96 hrs. Usually late. Smaller and grow more poorly than pneumo- or streptococci	

Libman considers these endocarditis-cocci as attenuated streptococci.
Rosenow regards them as attenuated pneumococci. Schottmüller regards them as *Streptococcus mitior* or *viridans.*

Prognosis.—The disease is nearly always fatal, but the fever may continue for months or even 1 to 2 years before death.

NOTE.—For further description and references, see Part VI.

(c) *Erysipelas*

Definition.—Erysipelas is an acute inflammation of the skin, spreading through the lymphatics, nearly always due to *Streptococcus hemolyticus.*

Symptoms—The streptococcus enters through some small lesion on skin or mucous membrane, very often on the face, following a scratch, insect bite, or an excoriation about the nose or lip. The erysipelatous dermatitis may occur on any part of the body from infection of a wound, or of an ulcer. It is not uncommon, in the new born, at the umbilicus.

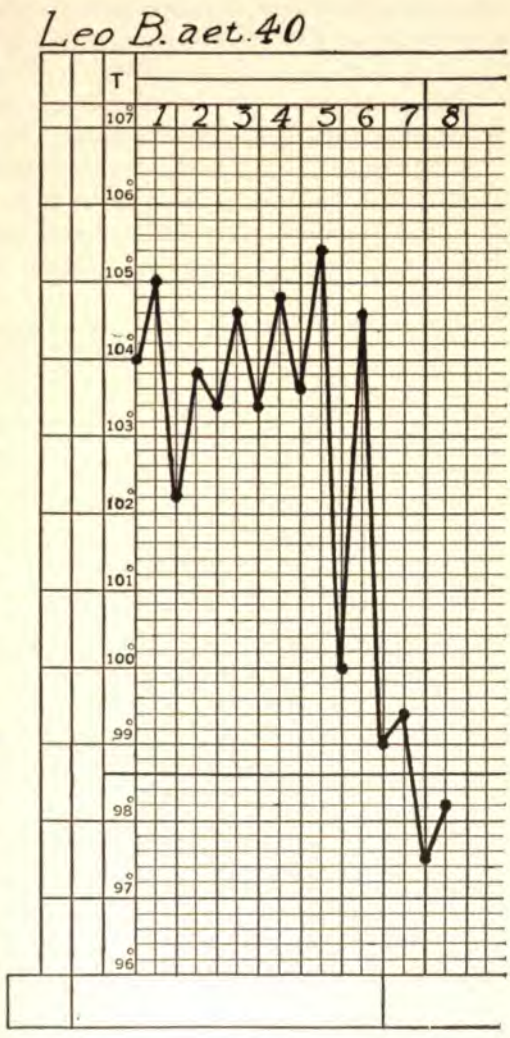

Fig. 58.—Erysipelas.

The incubation period varies in length from a few hours to 3 to 7 days. The onset is usually sudden, with chill, fever, and vomiting. A sharply limited area of redness appears on the skin of the face, trunk, or extremities. This area is swollen, hot, and tender. The surface is tense and often glazed; vesicle formation is common. In facial erysipelas the features are characteristically altered by the swelling; the nose broadens, the lips become thick, the ears huge and stiff, as if made of red wax. The eyes are swollen shut; but it is very rare to see any conjunctivitis. Though the spread is rapid, it is often checked where the skin is tight (chin, margin of hair, upper neck). The swelling and redness of the area first affected may disappear and desquamation begin while the disease is still

spreading at the margin. The course is often rapid, the disease terminating in from 4 to 8 days. More rarely, the process advances further and further and may wander over a large part of the body (*erysipelas migrans*). The adjacent lymph glands are swollen and tender. The fever, high at onset, is usually continuous or slightly remittent for an average of 4 to 6 days; it may end by crisis or by lysis. Ten per cent of the cases are afebrile. Leukocytosis is the rule. Headache, anorexia and weakness are usual. The patients are restless, and may be dull, or delirious (drinkers). Relapses are common. Erysipelas may affect the throat or tonsils; occasionally it involves the larynx, and causes edema of the glottis. The mortality varies from 4 to 7 per cent.

Complications.—Bronchitis, bronchopneumonia, septicemia, metastatic arthritis or meningitis, furunculosis.

Diagnosis.—Usually easy. Occasionally the disease is confused with phlegmon, anthrax, or erythema. It is not to be mistaken for the erysipeloid of Rosenbach (in which a butterfly-shaped area of redness appears over the nose and cheeks in butchers, cooks, etc.).

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(*d*) *Streptococcal Puerperal Sepsis*

Puerperal fever is the most important form of streptococcal sepsis. It is most often due to the aërobic *Streptococcus hemolyticus;* while, in septic abortion, the infection is most often caused by the anaërobic *Streptococcus putridus.* The general infection may follow any one of several forms of local streptococcus infection: (1) *endometritis;* (2) *thrombophlebitis,* in which there is a chill at the end of the first, or the beginning of the second week after delivery, followed by high fever and sweating, and later chills every two or three days; (3) *pelvic peritonitis* or *parametritis* (lymphogenous form of puerperal sepsis).

Diagnosis.—This is usually easy when the signs of infection follow a birth, or an abortion. Extragenital diseases like *typhoid, tuberculosis, malaria,* and *scarlet fever* must be ruled out. Gynecological examinations, blood cultures, and cultures from the lochia are helpful.

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(*e*) *Streptococcal Sinus Thrombosis* (*Otogenous Sepsis*)

Symptoms.—The onset is usually sudden, with nausea, vomiting, headache, vertigo, chills, and fever. Tenderness over the mastoid with swelling is frequently observed. If the thrombus extends into the jugular vein, it may be palpable in front of the M. sternocleidomastoideus. A blood culture from an arm vein often shows the presence of *Streptococcus hemolyticus.* Libman recommends simultaneous cultures from blood of an arm vein and from blood obtained by sinus puncture.

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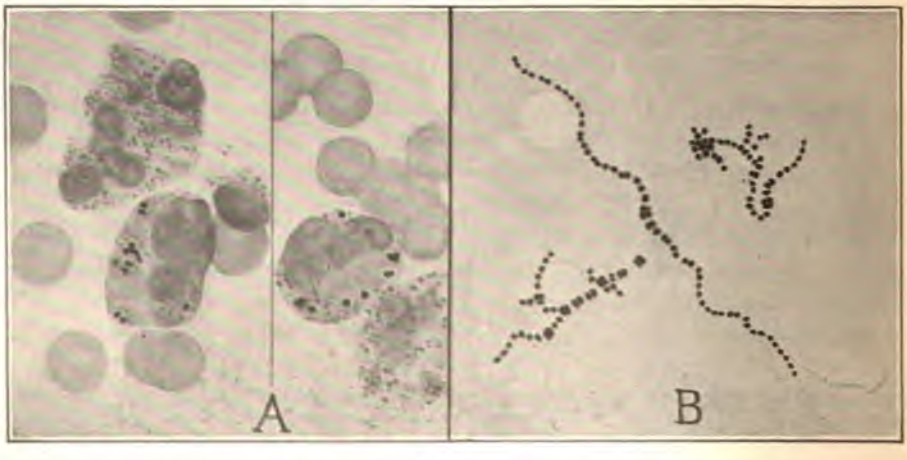
(*f*) *Streptococcal Angina*

Ordinary sore throats, especially acute tonsillitis, are very often due to *Streptococcus hemolyticus.* Not infrequently, they form the starting point of a general sepsis, of an endocarditis, of a metastatic arthritis, or of an embolic nephritis.

The absorption of streptococcus toxins (without bacteriæmia) not infrequently leads to diffuse renal intoxication (large white kidney).

A



B

Fig. 59.—(A) Swollen Glands of the Neck in Septic Sore Throat: (B) Streptococci from Septic Sore Throat. (Drawn by Max Broedel.) (After L. P. Hamburger, J. H. H. Bull.)

Recently, peculiar *epidemics of streptococcal angina*, with bubolike enlargement of the cervical lymph glands, have been met with in America, especially in Baltimore, in Boston, and in Chicago. In a number of these cases, a general streptococcal septicemia, or a streptococcal peritonitis, has been met with as a complication.

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(*g*) *Acute Rheumatic Fever*

(*Acute Articular Rheumatism; Polyarthritis rheumatica acuta*)

Definition.—Acute rheumatic fever is an acute, non-contagious, infectious disease, usually beginning with angina, and characterized by fever, sweating, and an excruciatingly painful, serous inflammation of a number of joints, which become involved one after the other, with strong tendency to complicating thrombo-endocarditis, the whole disease process, especially the pains, reacting promptly to salicylate therapy. It is sometimes followed (in children) by chorea.

Etiology.—The virus was, until recently, entirely unknown. Hundreds of careful blood cultures, in the clinic in which I work, were, up to the end of 1913, uniformly sterile, and cultures made from the joints were sterile. English observers (Poynton and Payne) had found a diplococcus in the blood, and many other microörganisms have been described in the disease. Recently, Rosenow (Chicago) has isolated streptococci from joints, tonsils, and regionary lymph glands, which, by animal passage and by other means, he believes he can convert into typical hemolytic streptococci on the one hand, and into pneumococci on the other. On animal inoculation, these

cocci give rise to polyarthritis, myocarditis, and myositis. This work is exceedingly interesting and further studies in the same direction should be closely watched.

My own observations had, up to the time of Rosenow's work, kept me skeptical regarding a bacterial etiology. I was strongly of the opinion that acute articular rheumatism was due to some virus wholly different from any ordinary form of bacterium, a virus that seemed to attack primarily the tonsils, with subsequent virusemia metastatic virus-infection of the joints and sometimes of the endocardium.

Rosenow is, however, such a careful worker, that any statement he makes must be given serious consideration. At my request, one of our staff, Dr. Arthur Bloomfield, went to Chicago, where Dr. Rosenow kindly instructed him in his technic of making cultures from the blood and from the lymph glands in acute and in chronic polyarthritis. On returning to the clinic in Baltimore, Dr. Bloomfield has been able, by these methods, to isolate from the blood and from the lymph glands, in arthritis cases, streptococci, apparently identical with those described by Rosenow. There can be no doubt that by Rosenow's method, bacteria can be grown from many patients when cultures made in the ordinary way remain sterile.

Rosenow had found in his studies on the transmutation of pneumococci and streptococci that oxygen pressure plays an important rôle in bringing about changes in these organisms; it occurred to him that the bacteria in rheumatic cases might be exceedingly sensitive to oxygen and that the negative cultures in acute rheumatism might be due to failure to supply and maintain the proper oxygen tension in the culture media. He devised a technic, by which in the same tube of medium, not only aërobic and anaërobic conditions are provided, but also all degrees (a gradient) of oxygen pressure between these two extremes. The blood, freed from hemoglobin and from complement, or the exudate from a joint, is mixed with ascites-dextrose agar (first melted and then cooled to a point just short of consolidation), in a tall test tube, so that on solidification, a tall column of solid inoculated medium results; at the surface, aërobic conditions exist; at the bottom, the conditions are anaërobic; in between, the inoculated material is exposed to a gradient of oxygen tensions. By this method Rosenow got pure cultures of streptococci from the joint fluid in acute rheumatism in 16 out of 19 non-fatal cases, and from the blood in 5 out of 8 cases.

These strains of streptococci all differ in one respect or another from *Streptococcus viridans*, on the one hand, and from *Streptococcus hemolyticus*, on the other. They vary in virulence; they produce much acid in media containing dextrose; they tend to change in their properties on cultivation; they grow better than ordinary streptococci at low temperatures; they are more virulent for frogs than are either pneumococci or ordinary streptococci. Injected into rabbits and dogs, they are said by Rosenow to exhibit not only an affinity simultaneously for the several serous membranes (endocardium, pericardium, and joint membranes), but also a tendency to localize in the experimental animals at sites corresponding roughly to the sites of the lesions in the human cases whence they were isolated. Thus with strains from human cases without myositis, the experimental animals did not develop myositis, while strains derived from myositic lesions in man gave rise to non-suppurative myositis and myocarditis in the animals, in addition to arthritis and endocarditis. After cultivation and animal passage, however, this localization-specificity is said soon to be lost. Rosenow (1912) believes that he can convert, by appropriate means, these rheumatic strains of streptococci into other members

of the streptococcus group and *vice versa*. His experiments on mutation make him believe that these and other streptococci, grown in symbiosis with other bacteria and under varying degrees of oxygen pressure, may acquire new properties; he thinks that streptococci may thus undergo change in the human body, in the tonsils, for example. It is his opinion, also, that the more chronic forms of arthritis, such as one called chronic progressive polyarthritis, are due to streptococci with distinctive cultural and pathogenic features, which are in keeping with the types of the disease in which they occur in man.

Rosenow's Technic.—Dr. Arthur Bloomfield has kindly furnished me with the following details. For the isolation from blood and tissues of organisms that do not grow readily under conditions of complete aërobiosis or anaërobiosis, Rosenow uses the following method:

1. Blood Cultures.—Fifteen to 30 c.c. of blood, drawn by venepuncture, are introduced into citrate solution to prevent clotting, and the mixture laked by adding about 10 volumes of sterile distilled water. This solution is now centrifuged at high speed for about 2 hours, the clear supernatant fluid decanted, and the sediment inoculated. Tubes of 1 per cent glucose agar (.5 per cent acid) are boiled for several minutes to drive off as much oxygen as possible, and then cooled to about 50° C. About $\frac{1}{5}$ volume of ascitic fluid, which has been heated at 60° C. for about 24 hours, is added, and small amounts of the blood sediment are now introduced with a sterile pipet. The tube is not shaken, but after thoroughly flaming the plug and the top of the tube, it is inverted once to distribute the inoculated material through it. The column in the tube is about 10 cm. high.

The colonies appear, after incubation, as opaque grey bodies and are easily distinguishable from the tissue particles which may be present in the tubes. To subculture the colonies, the tubes are broken and the organisms fished out and transferred to blood agar or to serum slants, or stabs may be made into solid tubes of ascites-dextrose agar.

2. Cultures from Tissues.—The lymph gland, or other piece of tissue, is dipped into boiling water for an instant to kill any bacteria on the surface, and is then immediately inserted into a sterile box containing a mortar, so arranged that, by means of an opening in the side to which a glove is attached, the tissue can be ground up under perfectly sterile conditions. A satisfactory apparatus can be improvised from a five-pound ether can. The fragments of tissue and the juice are next inoculated into the glucose-ascites-agar tubes in exactly the same way as for the blood sediment described above.

The principle of this method lies in the fact that varying grades of oxygen tension are offered to the organisms in addition to aërobic and anaërobic conditions.

The view of Sahli that acute articular rheumatism is a sepsis due to an attenuated staphylococcus or streptococcus had been less in favor since the conception of *acute infectious pseudorheumatisms* has had more acceptance. Rosenow's results lend new interest to Sahli's view.

The disease is most common in youth and during adolescence; it is not very common after middle life, though its residues (valvular disease of the heart; adherent pericardium) are often seen.

Symptoms.—The *onset* is usually sudden, often after *tonsillitis* (70–80 per cent of the cases); or a short period of arthralgia, myalgia, and malaise, with fever that rises rapidly may precede the outspoken joint involvement. *Inflammation of several joints* develops, usually within 24–48 hours, the disease jumping from joint to joint characteristically, causing swelling, redness and excruciating pain, especially when the joints are moved. The

swelling is mainly periarticular, but effusion into the joint is not uncommon. The order of frequency of involvement is as follows: knee, ankle, shoulder, wrist, elbow, hip, hand, and foot. The sternoclavicular, temporomaxillary, and vertebral joints are not, as a rule, involved. The inflammation subsides in one joint while increasing in others, and, after the arthritis has subsided, no residual deformities remain. There is a great tendency to recurrences.

The *fever* is irregular, being usually markedly remittent; defervescence is by lysis. Tachycardia may be pronounced. An apical systolic bruit is frequently heard, even in the absence of endocarditis.

Characteristic, in typical cases, are the profuse *sour sweats,* as a result of which sudaminal vesicles (*miliaria crystallina* and, less often, *miliaria rubra*) develop. Simple erythema, erythema multiforme and nodosum, urticaria, or purpura may be associated. *Subcutaneous fibroid nodules* are sometimes seen, especially in children; they are most numerous along fasciæ, and on the tendons about the fingers, hands, wrists, scapulæ, elbows, knees, and spine.

Anorexia, thirst, and perspiration are prominent symptoms. There is commonly a *febrile nephropathy* with very acid urine. A marked secondary *anemia* quickly develops, and the blood shows a *leukocytosis* (10,000–18,000), with P. M. N. increase from the beginning. In chorea, the eosinophils may be increased to 10 per cent (Macalister).

The **course** is very variable; the duration is probably not influenced by salicylates; most cases continue for several weeks, but there are shorter attacks lasting 1–2 weeks.

The **mortality** is low (2–4 per cent), but the outlook for the distant future is often gloomy on account of the frequency of an associated endocarditis, myocarditis, or pancarditis.

Complications.—*Endocarditis* is extremely common; it affects especially the mitral valve, but sometimes both the mitral and the aortic valves, and usually leads to permanent valvular lesions (stenoses; insufficiencies); *pericarditis* and *myocarditis* are common; more rarely *pleuritis* is seen; occasionally, hemorrhagic *nephritis,* or *peritonitis,* develops. In one group of cases, *erythema multiforme* is common. A purpuric form is sometimes met with (*peliosis rheumatica*). In children, *chorea minor* is a frequent complication or sequel; it seems to be due to a cerebral localization of the causative streptococci, perhaps of a modified strain (Dick and Rothstein, 1913). A very dangerous complication is the *rheumatic hyperpyrexia,* or cerebral rheumatism (not to be confused with salicylate delirium!), in which the temperature may rapidly rise to 106° or to 108° F., with delirium, convulsions, coma, and death. Recurring rheumatic *iritis* is not uncommon. Old rheumatic hearts are especially predisposed to secondary septic infection (*endocarditis lenta,* etc.). Enlargement and tenderness of the thyroid are not uncommon (Vincent); some authors regard acute rheu-

matic fever as the commonest provocative cause of Graves's disease (Mouriquand and Bouchut).

Diagnosis.—In children, and in young adults, the typical picture, with tonsillitis, fever, and polyarthritis flying from joint to joint, reacting promptly to salicylates, and prone to endocardial complications, is not difficult to recognize. It is sometimes hard to rule out an *acute infectious pseudorheumatism* (Bouchard), or so-called *rheumatoid* disease (Gerhardt), including the polyarthritides due to gonococci, pneumococci, etc. The *arthropathy following serum injections* (diphtheria antitoxin) may be confused with acute rheumatic fever.

Sometimes, the early stage of a *primary chronic progressive polyarthritis* may be so acute as to simulate acute rheumatic fever, but, in this disease, the jaw joint, the sternoclavicular joint, and the cervical spine are not infrequently affected—joints that are only rarely involved in acute rheumatic fever. The quick appearance of muscular atrophies, and the absence of tendency to endocarditis and to other serous membrane involvements help to differentiate.

The *postscarlatinal polyarthritis* is not a true polyarthritis rheumatica.

Acute osteomyelitis can be distinguished (1) by the positive blood culture for staphylococci, and (2) by röntgenograms of the bones.

Acute gout rarely offers difficulty in diagnosis (nocturnal onset; sites of predilection; family history; disturbed purin metabolism; response to colchicum).

Whether a **chronic articular rheumatism** due to the same virus as that which causes true rheumatic fever ever occurs, is much disputed (T. McCrae). The question can scarcely be settled until the virus of acute rheumatic fever is definitely established, and its presence or absence in the chronic processes determined. Some think that Jaccoud's *rheumatismus fibrosus* is a true chronic rheumatism. The tendency now is to reserve the term *rheumatism* for diseases caused by the virus that is responsible for acute rheumatic fever, and not to apply it to other forms of arthropathy.

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(*h*) *Chronic Streptococcal Arthritis*

Recent bacteriological studies have shown that a certain proportion of the cases of chronic arthritis are due to infection with *Streptococcus*. It is not often possible to demonstrate the streptococcus in these cases in the joints themselves except at autopsy, but now and then cultures from the regional lymph glands reveal the presence of numbers of these bacteria. In such cases the primary focus of streptococcus infection should be sought for.

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2. Diseases Due to Staphylococci

The Pathogenic Staphylococci.—These include the *Staphylococcus aureus,* the *Staphylococcus albus,* and the *Staphylococcus citreus.* Of these, the *aureus* is the most pathogenic. The albus is always present in the human skin, and is often spoken of as the "skin-coccus"; it sometimes gives rise to local and to general infections. The individual cocci are round, smaller than streptococci, and are usually arranged in grapelike bunches. They grow well on ordinary media, liquefying gelatin. They stain with ordinary anilin dyes, and are Gram-positive. On blood-agar plates, two kinds of colonies are seen at the end of 24 hours:—(1) in the depth, black points without hemolytic areas about them, and (2) on the surface, white and golden-yellow colonies surrounded by clear areas, due to absorption of hemoglobin. These surface colonies show hemolysis owing to the presence of more oxygen there than in the depth.

Staphylococci give rise to a poison which hemolyses the red corpuscles (*staphylolysin*), and to another which destroys the white corpuscles (*leukocidin*). The principal poisoning in staphylococcus infections, however, seems to be due to *endotoxins* arising from the bodies of the staphylococci themselves.

Portals of Entry.—Those most often concerned are (1) wounds, tears, punctures, pricks, or scratches of the *skin*, followed by local inflammation (furunculosis, carbuncles, panaritium, acne) and sometimes by general sepsis; (2) the mucous membrane of the *urogenital tract* (bladder, pelvic organs, and kidney), and (3) the mucous membrane of the *throat* (tonsils, pharynx).

Multiple purulent *metastases* are very common in staphylococcus sepsis (lung abscess, endocarditis, abscesses in heart, spleen, kidneys, joints, and bone-marrow). When the cocci go over into the blood, the *blood culture* is sometimes positive, but is often negative, as the cocci are quickly removed from the blood by the organs (in contrast with streptococcus sepsis).

(*a*) *Staphylococcal Septicemia*

Symptoms.—There is high fever, usually continuous, or slightly remittent, rarely accompanied by chills; often relative bradycardia; palpable spleen; hyperleukocytosis; delirium; signs of metastases (lung abscess, septic endocarditis, polyarthritis, meningitis).

Diagnosis.—Blood culture; urine culture; finding of primary focus of infection; cultures from metastatic abscesses.

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(*b*) *Acute and Chronic Osteomyelitis*

Etiology.—Osteomyelitis is nearly always due to infection with *Staphylococcus aureus;* occasionally it may be due to *streptococci,* or to *pneumococci.*

Symptoms.—The onset is usually acute, with fever, chills, and pains in one or more of the bones (femur, tibia), followed by swelling of the part, and later, by necrosis and sequestrum-formation. There is often pus formation, with abscess.

Diagnosis.—Blood cultures are nearly always positive at some stage of the disease. Röntgenograms are helpful in the diagnosis of this condition.

Differential Diagnosis.—A number of conditions should be ruled out especially in children (fracture; Barlow's disease with its painful subperiosteal hemorrhages). In the more chronic forms of osteomyelitis in which the swelling arises gradually, the patient being, perhaps, afebrile, the differential diagnosis is usually more difficult than in the acute cases. In addition to chronic osteomyelitis due to staphylococci or streptococci, we must think of *cold abscess,* of *sparotrichosis,* of *neoplasm,* and of *gumma.* (See Part XI.)

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(c) *Furunculosis*

In this condition, local areas of inflammation occur in the subcutaneous tissue. In the center of each area, containing masses of staphylococci, is a core of necrotic tissue; outside this there is edema, with leukocytic infiltration. As the boil ripens, the tissues undergo softening, and the leukocytes increase in number with pus formation. The **boil** will often break, if left to itself, or if it be poulticed. The infection usually begins in a hair follicle. Sites of predilection are the back of the neck, the nates, the external genitalia, the axillæ and the external auditory canal. Diabetes strongly predisposes to such infections and widespread furunculosis is also common during convalescence from typhoid fever. A furuncle on the upper lip is especially dangerous owing to the frequent involvement of the facial veins with pyemia as a sequel. The so-called **carbuncle** of the neck may consist of a single boil, or of a group of conglomerate furuncles (common in the senile, and in diabetes). Before the bacteriological era, such staphylomycotic carbuncles were sometimes confused with anthrax.

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3. Diseases Due to Pneumococci

The Pathogenic Pneumococci.—The *Diplococcus pneumoniæ* (Weichselbaum), *Pneumococcus* (Fraenkel) or *Micrococcus lanceolatus* (Welch) is met with usually in pairs, each individual coccus being lancet-shaped; sometimes chains of 4 to 6 occur. It stains easily with ordinary basic anilin dyes and is Gram-positive. In preparations made from the tissues or fluids of infected animals and man, it is seen to be surrounded by a capsule, each capsule inclosing 2 cocci; in cultures it often grows without capsule.

Growth will occur, though feebly, on ordinary media at 37° C. The pneumococcus grows much better on media containing human serum. It dies out easily, unless frequently transplanted, though it may live for some time in dry sputum or in dry blood.

In most cases, it is easily recognizable by its morphology, but it is best isolated by the injection of suspected material into a mouse, or a rabbit; in these animals it quickly gives rise to pneumococcus septicemia, and may, after 24 hours, be obtained in pure culture from the blood. Normal sputum usually contains the pneumococcus (hence the sputum septicemia [Sternberg; Pasteur] on injection of sputum into rabbits, or mice); in

man, it is a harmless occupant of the mouth cavity in 50–70 per cent of normal individuals.

Differentiation of Pneumococci from Streptococci.—Blood-agar plates are helpful. The *pneumococcus* differs from *Streptococcus hemolyticus* in that the colonies grow green and are not surrounded by hemolytic zones. It differs from *Streptococcus viridans* in (1) its lancet shape, (2) its capsule formation in animals, (3) the more intense green color of its colonies on blood-agar, (4) its stronger growth in the depth of blood-agar, (5) its inability to precipitate serum-glucose-agar, and (6) its power of fermenting inulin. E. C. Rosenow believes that he can, by transfer methods, convert certain streptococci into pneumococci and *vice versa.*

Mice and rabbits are most susceptible to pneumococcus infection, minute amounts of virulent pneumococci killing them within three days, often within 24 hours, from septicemia.

Strains of Pneumococci.—Cole and Dochez, and Dochez and Gillespie, Rockefeller Hosp., N. Y., confirming and extending the earlier work of Eyre and Washbourne, and of Neufeld and Haendel, have shown that pneumococci, isolated from pneumonia, are divisible into *four groups.* This fact may prove to be important in the development of a specific therapy, as powerful antisera have been produced against two of the groups.

The cocci belonging to each of the first two groups are said to be specific, as far as the immunity to which they give rise is concerned. The immune serum (horse) arising from injections of a pneumococcus belonging to **Group I,** has a specific protective action against all pneumococci belonging to Group I, but does not protect against pneumococci belonging to Groups II, III, or IV. Similarly, a pneumococcus belonging to **Group II** will yield, on injection, a serum protective against all cocci belonging to Group II, but against no other cocci. **Group III** contains all the pneumococci of the type of *Pneumococcus mucosus.* On injection it has not been found possible to produce a protective serum against any member of this group. **Group IV** includes all pneumococci against which the serums prepared by injection of pneumococci belonging to Groups I and II are ineffective and which by cultural or pathogenic qualities can be shown not to belong in Group III. An immune serum prepared by injection of a pneumococcus belonging to Group IV is protective against the strain used, but will not protect against other strains belonging to Group IV, nor will it protect against the races belonging to Groups I, II, and III. The pneumococci belonging in Groups I and II can also be easily recognized by agglutination tests made with the respective immune sera. Pneumococci belonging to Group III are easily recognized by their cultural and pathogenic characters. Membership in Group IV is determined by exclusion.

P. W. Clough has demonstrated an increase of phagocytic power for the homologous (virulent) pneumococcus in the blood serum of patients after the crisis in pneumonia.

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(*a*) *Croupous Pneumonia* (*Lobar Pneumonia*)

This disease is nearly always due to some member of one or another of the four groups of pneumococci above described. In a few cases the causal agent is Friedländer's bacillus. (For symptoms, diagnosis, etc., see Diagnosis of Diseases of the Lungs.)

(*b*) *Pneumococcal Septicemia*

Definition.—In human pneumococcus infections, primarily local, the cocci may go over into the blood and multiply there. If only a few reach the blood, and there be no marked multiplication, we speak of a "pneumococcus bacteriemia." But the blood may contain a large and increasing number of the cocci; we then speak of "pneumococcus sepsis." Such a pneumococcus sepsis may follow pneumonia, otitis media, an angina, or a cholecystitis. The severer toxic symptoms in fatal cases of pneumonia probably depend, in most instances, on pneumococcus sepsis.

Symptoms.—In pneumococcus sepsis, the fever is, as a rule, high and continuous, though in some cases it is markedly intermittent. Suppurative metastases are not uncommon, and are usually fatal. Ulcerative pneumococcus *endocarditis* and pneumococcus *meningitis* are serious complications. Occasionally, a metastatic pneumococcus *arthritis* is met with; it is usually suppurative.

4. Diseases Due to Gonococci

The Gonococcus (Neisser).—This is a biscuit-shaped or coffee-bean-shaped coccus, occurring in pairs (diplococci), the adjacent edges of the cocci in each pair being flattened. In gonococcal inflammations, the protoplasm of the leukocytes is often crowded with pairs of gonococci (intracellular cocci).

The gonococcus stains with ordinary anilin dyes, but it is Gram-negative, an important point in diagnosis. In fixing the smear, overheating should be avoided; during the Gram-staining, the stain should not be allowed to evaporate; the decolorization in alcohol should be thorough.

The gonococcus does not grow well on ordinary media. It grows best on more highly albuminous media, and especially well on ascites–agar, or hydrocele-fluid agar, though it grows fairly well on blood-agar without

hemolysis. The nutrient medium should be neutral or very feebly acid. The optimal temperature for growth is 35°–37° C.; a rise above this endangers the life of the organism, and, as E. E. Irons suggests, it is well to set the regulator of the thermostat at 35° C., so that, if a slight unavoidable rise of temperature occurs, it will not be great enough to kill the culture.

The organisms are easily demonstrable in the pus of gonorrheal urethritis or conjunctivitis, and in the exudate of gonococcal endocarditis and gonococcal arthritis. In smears stained with alkaline methylene blue, they are visible chiefly as intracellular cocci. If such cocci are found also to be Gram-negative they are probably gonococci. Care must be taken not to confuse the gonococcus with (1) the meningococcus, (2) non-hemolyzing streptococci, (3) micrococcus catarrhalis, (4) coccoid forms of B. coli, and (5) the pseudo-gonococcus.

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(*a*) *Gonococcal Inflammations of the Urogenital Organs*

The gonococcus is a common cause of urethritis (see Gonorrhea), prostatitis, cystitis, epididymitis, pyelitis, vulvovaginitis, endometritis, pelvic peritonitis, and salpingitis. In the male, gonococcal epididymitis, and in the female, gonococcal salpingitis, are among the commonest causes of sterility. (See Part X.)

(*b*) *Gonococcal Conjunctivitis* (*Ophthalmia neonatorum*)

This is one of the commonest causes of blindness. About a quarter of the blind children in the schools for the blind in the United States owe their blindness to gonococcal infections. It is rarer now than formerly, for many obstetricians have adopted Credé's method (1881) of instilling one or two drops of a solution of silver nitrate into the conjunctional sac of the newborn, irrespective of whether gonorrhea is supposed to be present in the mother or not. A single instillation of a 1 per cent solution in each eye has been found to be sufficient; the stronger solution may excite a "silver catarrh."

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(*c*) *Gonococcal Endocarditis* (*Endocarditis gonorrheica*)

This is often one of the most prominent symptoms of a general **gonococcus sepsis.** It is usually associated with gonococcal polyarthritis. The endocarditis may be combined with pericarditis and myocarditis due to the same coccus. A gonococcal pleuritis is occasionally observed.

Gonococci were isolated from the blood of living patients suffering from gonococcal endocarditis by Thayer and Lazear and by Thayer and Blumer (1895). They were demonstrated in blood cultures in cases of gonococcal arthritis by Hewes (1894) and by Ahmaner.

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(*d*) *Gonococcal Polyarthritis* (*Gonorrheal Rheumatism*)

Here we deal with a metastatic infection, usually of several joints, following gonococcal inflammation of the urogenital system, or, rarely, of the conjunctiva. At the outset a number of joints are involved (polyarthritis); later, the inflammation becomes most marked, as a rule, in a single joint (monarthritis), most often one knee-joint, or one ankle-joint. Occasion

ally, a joint suppurates. The symptoms are but little relieved by salicylates or by potassium iodid. Exacerbations and recurrences are very common and often run parallel to exacerbations of the primary urethritis or prostatitis. The complement-fixation test is positive.

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(*e*) *Gonococcal Iritis*

This occurs not infrequently as a metastatic complication in gonococcal polyarthritis, or after it. Recurrences of the iritis are common; it is not certain whether they represent a renewal of the infection or an allergic local reaction due to the sudden setting free of gonococcus protein elsewhere in the body.

5. Diseases Due to Meningococci

Meningococcus, or Diplococcus intracellularis meningitidis (Weichselbaum).—This organism closely resembles the gonococcus in its biscuit-shaped morphology. In a meningeal exudate, obtained by lumbar puncture, the cocci are chiefly intracellular, though some extracellular cocci may also be seen. The meningococcus stains easily with methylene blue and with other basic anilin dyes. It is Gram-negative. In cultures, the size of the individual cocci is variable; along with small forms, one sees some giant cocci, three or four times as large as the others. The individual cocci also take the stain with variable intensity.

This coccus grows best at 37° C., and on media containing human or animal serum. Blood-agar, ascites-agar, and hydrocele-agar are excellent media for the cultivation of it. The growth is particularly good on ascites-agar to which some glucose has been added. In using blood-agar as a medium, the proportion of 2 c.c. liquid agar to 3 c.c. human blood is most suitable.

The meningococcus quickly dies out in cultures, unless transplanted every 5 days. It is also very sensitive to light and to drying. It is almost non-pathogenic for animals, except young guinea-pigs and mice. Injected into the subarachnoid space of monkeys, it causes meningitis. Dead cocci, injected into rabbits and horses in increasing doses, yield a serum rich in

specific agglutinin; this is most helpful in the recognition of suspicious colonies, grown on ascites-agar.

In testing for meningococcus carriers by cultures from the pharynx, a number of organisms must be ruled out (*Micrococcus catarrhalis, Diplococcus crassus, Diplococcus flavus, and Micrococcus cinereus*). For methods, see special texts.

(*a*) *Epidemic Cerebrospinal Meningitis*

(*Cerebrospinal Fever, Meningitis meningococcica*)

Definition.—An acute contagious disease, usually occurring in epidemics; due to infection of the leptomeninges with the meningococcus, which is demonstrable in fluid obtained by lumbar puncture.

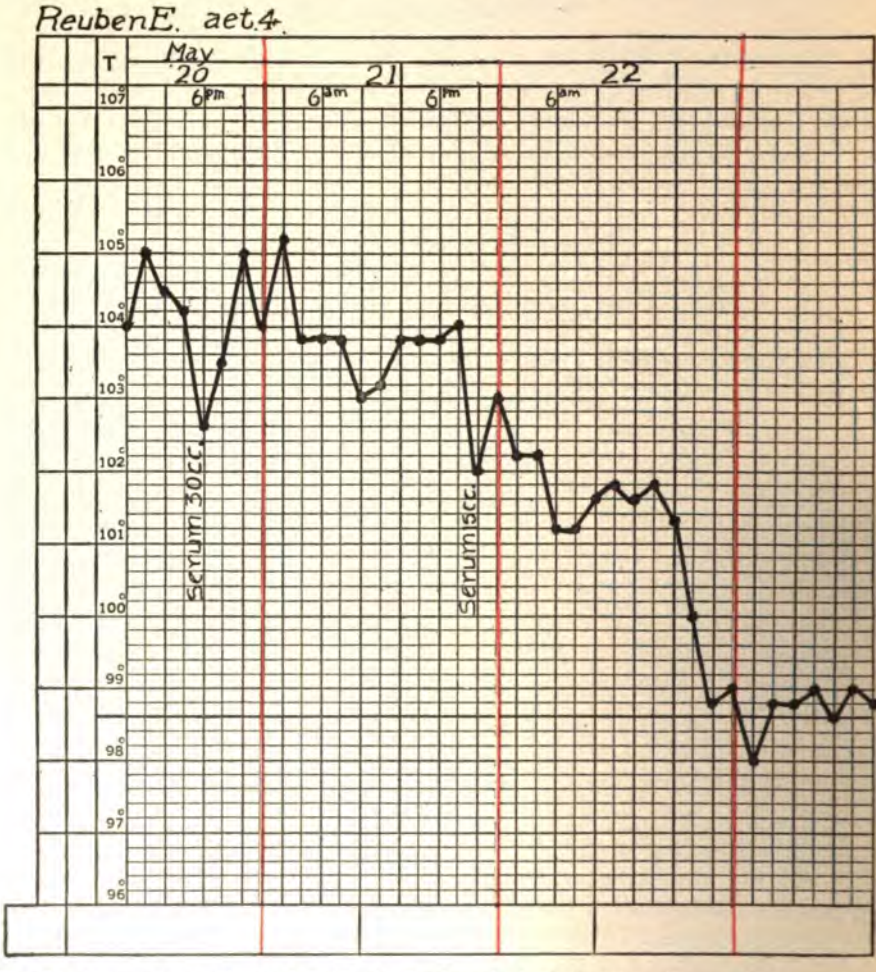

Fig. 60.—Temperature Chart of Epidemic Cerebrospinal Meningitis. (Personal Observation.)

Epidemiology.—The disease is spread, apparently, less by direct contact with the patient than by the intermediation of so-called healthy *meningococcus carriers,* that is, healthy individuals who harbor meningococci in the nasopharynx. In mining districts, especially, the father of a sick child carries the meningococcus to the mines, and contaminates other fathers, who, as meningococcus carriers, on going to their homes, infect their own children.

Fig. 61.—Epidemic Cerebrospinal Meningitis—Retraction of the Neck. (After J. Ibrahim, in E. Feer's "Lehrb. d. Kinderheilkunde," published by G. Fischer, Jena.)

Incubation Period.—This is usually short, rarely exceeding 2 or 3 days.

Symptoms.—The onset is sudden, with violent headache, vomiting, STIFFNESS IN THE NECK, chills, and fever (in contrast with the slow onset in tuberculous meningitis). The blood shows a *polymorphonuclear leukocytosis* (10,000–20,000).

When the disease is fully developed, the pain in the head, photophobia, irritability, restlessness, vomiting, rigidity of the neck, general *cutaneous hyperesthesia,* rigidity of the legs, and KERNIG'S SIGN (inability to assume or to be placed in a sitting position without flexion at the hip and knee) are very characteristic. Muscular rigidity often leads to orthotonus, or to opisthotonus. Tremors of muscles, tonic and clonic spasms, ankle- and patellar-clonus, are common.

Fig. 62.—Epidemic Cerebrospinal Meningitis. (Med. Service, J. H. H.)

BRUDZINSKI'S SIGNS, (1) flexion of head on chest, causing flexion at the hips and knees (*frog sign*), and (2) flexion of one thigh on abdomen, causing similar flexion on the opposite side (*contralateral reflex*), are present. Symptoms referable to involvement of the individual cerebral nerves (eye muscle paralyses, optic neuritis, deafness) are often seen, but less frequently than in tuberculous meningitis. Occasionally, focal symptoms (hemiplegia, convulsions) occur. Delirium is common, often followed by stupor and coma. The *fever* is remittent or intermittent. The reflexes may be either increased or diminished; the patellar reflexes are often absent; Babinski's "phenomenon of the toes" may be positive, in adults, in the second week of the disease. A measles-like EXANTHEM, or roseola, is sometimes seen and petechiæ are common (spotted fever). *Herpes* of the face, lips and ears—usually extensive—is present in the majority of cases, except in children under 3 years of age, in whom it does not occur.

Fig. 63.—Brudzinski's "Identical Reflex" or "Frog Sign" in Meningitis. Method of Eliciting it by Flexing the Head on the Trunk. (From W. P. Northrup's Article, J. Am. M. Ass.)

Fig. 64.—Brudzinski's "Contralateral Reflex" in Meningitis. Method of Eliciting It. Passive Flexion of One Leg Causes Reflex Flexion of the Other Leg. (From W. P. Northrup's Article, J. Am. M. Ass.)

Complications.—A large number of different complications may occur; the commonest are polyarthritis, endocarditis, and bronchopneumonia.

Course of the Disease.—This varies all the way from the extremely acute type (*foudroyant*) known as MENINGITIS SIDERANS (in which death occurs in a few hours), to the protracted cases with prolonged meningeal suppuration and intermittent course. In the majority of cases, the convalescence sets in within a week, or death occurs before that time. In the protracted cases, HYDROCEPHALUS INTERNUS often develops; the patients become afebrile, emaciate rapidly, suffer from flexion-contractures of the lower extremities, and periodic vomiting.

In some cases, especially in children, the symptoms are peculiar, in that rigidity of the neck and Kernig's sign are absent. In such ATYPICAL FORMS, bulging of the fontanelles, and hyperalgesia on passive move-

ments of the legs, would lead one to make a lumbar puncture, especially in an epidemic.

Diagnosis.—In outspoken cases, especially in epidemics, the disease can scarcely be overlooked. In sporadic cases, and in atypical forms, the disease may go unrecognized unless lumbar puncture is done. The *cerebrospinal fluid* contains many polymorphonuclear leukocytes with intracellular (and extracellular), Gram-negative, meningococci.

Differential Diagnosis.—1. From *meningismus* (in typhoid, pneumonia, scarlet fever, etc.). In this, there may be rigidity of the neck, a positive Kernig's sign, hyperesthesia, and increased pressure of cerebrospinal fluid, *but the fluid contains neither pus cells nor bacteria.* In typhoid, the leukopenia and the positive blood culture are helpful in differentiation.

2. From *secondary meningitides,* following otitis media, paranasal sinusitis, etc. (streptococci, staphylococci, pneumococci, influenza bacilli). The bacteriological examination of the fluid (Gram-positive cocci; bacilli) distinguishes these from meningococcus infections.

3. From *tuberculous meningitis.* In this the onset is slow, herpes is usually absent, the spinal fluid may be clear, or only slightly turbid, and the sediment consists chiefly of mononuclear lymphocytes, not of polymorphonuclear leukocytes. Tubercle bacilli can often be demonstrated in the fluid obtained by lumbar puncture.

Sequelæ.—These, like the mortality, have been greatly reduced since the introduction of the treatment with Flexner's antimeningitis serum. Formerly, hydrocephalus, deafness, blindness, paralyses and imbecility were common sequels.

The *mortality* has been reduced by the serum treatment from 75 per cent to about 25 per cent. When epidemics prevail, immunization by dead cultures (Sophian and Black) might be considered as a measure of personal prophylaxis.

(*b*) *Meningococcal Arthritis*

(*Polyarthritis meningococcica*)

This is occasionally met with as a complication of cerebrospinal meningitis; it may also occur in the absence of meningitis.

(*c*) *Meningococcal Sepsis*

In the bibliography an increasing number of reports on meningococcal sepsis are met with, in which the meningococcus has been grown in blood cultures.

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6. Diseases Due to the Micrococcus melitensis

The Micrococcus melitensis, isolated by Bruce (1887), is a very small coccus. It is Gram-negative, and grows best on 20 per cent ascites-agar. It does not liquefy gelatin. It is pathogenic for monkeys, and gives rise in these, and in rabbits, to specific agglutinins. It is one of those micro-organisms that are most often the cause of accidental infections in bacteriological laboratories; thus, MacFayden lost his life from infection in the laboratory with *Micrococcus melitensis.* The coccus can be killed in milk by heating at 60° C. for 20 minutes (M. J. Rosenau).

(*a*) *Undulant Fever*

(*Malta Fever, Mediterranean Fever*)

Definition.—This is a septicemia, with chronic course, due to *Micrococcus melitensis,* and characterized by periods of fever, interrupted by apyretic intervals; hence the name "undulant fever."

Occurrence.—It is met with on the shores of the Mediterranean Sea, and in various tropical countries (Asia, Africa, America). An endemic center of the disease exists in a goat-raising section along the Rio Grande in Texas (Gentry and Ferenbaugh).

Portals of Entry.—It gains entrance chiefly by way of the alimentary tract, from drinking raw goats' milk containing the cocci; occasionally, by insect bites, or by contact (urine; dust).

Incubation Period.—This is 6 days, as proven by laboratory infection.

Symptoms.—These are indefinite at the onset (headache; anorexia; tired feeling in the limbs). The temperature rises gradually, though occasionally, the onset is sudden, with chills. Sweating, nausea, and insomnia are common. The abdomen is tender; constipation is marked; sometimes there is irregular diarrhea. In mild cases, the temperature may gradually fall at the end of 10 days. In severer cases, it lasts longer. After a few days of apparent convalescence, the temperature, in the majority of cases, rises again and remains elevated for 2 or 3 weeks. The patient grows anemic, and the spleen becomes enlarged and tender. The blood shows a leukopenia. Tenderness and swelling of the joints, and metastatic orchitis are common complications. The hair often falls out. Periods of fever and of apyrexia may alternate for months.

Diagnosis.—This is easy, if blood culture be made (*Micrococcus melitensis*). In the recognition of the coccus, the agglutination test (Konrich), and the complement-fixation test (Sicre) are helpful.

Differential Diagnosis.—(1) From *typhoid fever* and *paratyphoid;* (2) from *malaria;* (3) from acute and subacute *rheumatic fever,* and from *infectious arthritis.*

Prognosis.—In general, the outlook is favorable, the mortality being only about 2 per cent.

Prophylaxis.—Cows and goats become infected and their milk, when taken unboiled, causes the disease in human beings (English Mediterranean Fever Commission). The disease usually disappears from a community, if only boiled milk is taken, though infection may occasionally arise in other ways than through milk. The urine of patients should be disinfected.

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B. Diseases Due to Bacilli

1. Diseases Due to the Pneumobacillus (Friedländer)

Pneumobacillus (Friedländer).—This is a short, plump, encapsulated rod, which forms a naillike growth on gelatin at room temperature and is pathogenic for rabbits.

It occasionally causes a *croupous pneumonia;* it has also been found as a cause of *serositis,* and of *meningitis.*

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2. Diseases Due to the Scleroma Bacillus

Bacillus of Rhinoscleroma (von Frisch).—This bacillus closely resembles Friedländer's pneumobacillus, but is less virulent for animals. It is the cause of rhinoscleroma.

(*a*) *Rhinoscleroma*

This is a chronic, fatal disease of the air passages, infiltrating (in the form of bluish-red hard nodules) the skin and the mucous membrane of the nose, mouth, palate, pharynx, larynx, or external auditory canal. The infiltrations may feel as hard as ivory. In the nose, they lead to narrowing of the nasal cavities, and obstruct the breathing. The disease belongs among the "infectious granulomata" (along with tubercle, gumma, etc.). The nodules of rhinoscleroma show, however, no tendency to later softening.

The histology of the infiltrated area is characteristic (masses of plasma cells, together with groups of large clear cells (dropsical degeneration) containing the scleroma bacilli).

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3. Diseases Due to the Anthrax Bacillus

Anthrax Bacillus.—The *Bacillus anthracis* is a large, straight, non-motile rod occurring singly or in chains, in cultures often assuming a thread form. It stains easily with basic anilin dyes, and is Gram-positive. Outside the body, spore forms that are very resistant develop. The bacilli do not sporulate except in the presence of oxygen.

The bacilli are pathogenic for many animals (especially, cattle and sheep).

(*a*) *Human Anthrax*

Men are usually infected from hides, from wool, or from rags. The spores may infect the *skin* (anthrax carbuncle, malignant pustule, anthrax edema) or they (or the bacilli in raw meat) may be swallowed and give rise to *intestinal anthrax,* with symptoms of severe hemorrhagic enteritis. In a third form, the spores may be inhaled and give rise to *pulmonary anthrax* (woolsorter's disease; rag-picker's disease) characterized by hemorrhagic pneumonia, hemorrhagic pleurisy, and mediastinitis.

In all three forms of anthrax, the bacilli may spread through the lymphatics, and reach the blood, giving rise to *anthrax septicemia.*

Laboratory workers, and veterinarians, should exercise the greatest care in autopsying anthrax cadavers (rubber gloves).

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4. Disease Due to the Bacillus of Malignant Edema

Bacillus of Malignant Edema.—This resembles the anthrax bacillus in its shape (rods, threads). It also is Gram-positive. It differs from the anthrax bacillus in being strictly anaërobic.

In human beings it can, though rarely, give rise to a form of *gas gangrene,* resembling that due to the gas bacillus of Welch.

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5. Disease Due to the Gas Bacillus (Welch and Nuttall)

Bacillus aërogenes capsulatus (Welch and Nuttall).—This is commonly known as the gas bacillus, and is somewhat similar in form to the anthrax bacillus. It is Gram-positive, often shows capsule formation, is strictly anaërobic, and is pathogenic for guinea-pigs and for sparrows. E. Fraenkel's *Bacillus phlegmonis emphysematosae* is probably identical with Welch's bacillus.

(*a*) *Gas Gangrene* (*Hospital Gangrene*)

This disease, formerly so common as a complicating infection of wounds in the surgical wards of hospitals, is now very rare. It is, however, occasionally seen, and I saw it, when in Manila in 1899, follow a bullet wound in an unfortunate American soldier. Reports indicate that the infection has been met with among the wounded in the great war now going on in Europe.

The tissues swell, become discolored, and crackle under the finger. On incision, a turbid, sanguinolent, dirty-looking exudate is visible, in smears of which the thick gas bacilli are visible. The gas bacillus can also cause distention of the uterus in puerperal infection (*tympania uteri*); it may also give rise to *gas cysts* in the lymph vessels of the vagina (*colpohyperplasia cystica*).

The gas bacillus is, however, much more frequently met with at autopsy in the so-called *frothy organs,* or *foamy* organs (liver, spleen, kidneys) in which spherical cavities due to post mortem multiplication of the bacilli with gas formation are seen. The brain and liver, on section, may show holes like those of Swiss cheese.

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6. Diseases Due to the Tetanus Bacillus

Tetanus Bacillus.—*Bacillus tetani* (Nicolaier, 1884) is characterized by the presence of a terminal spore, which makes it resemble in form a nail or a pin. It is slightly motile, Gram-positive, strictly anaërobic, and pathogenic for animals. It was first grown in pure anaërobic culture by Kitasato (1887), who proved that it multiplies *in loco*, giving rise to a powerful toxin (*tetanus toxin*), which extends along the nerves to the nerve centers and causes a fatal intoxication of the brain unless early neutralized by *tetanus antitoxin*. The normal habitat of *B. tetani* is the intestinal tract of herbivorous animals, hence its occurrence in manure, in garden earth, in street dust, etc. The house fly may help to distribute tetanus spores. The spores are very resistant.

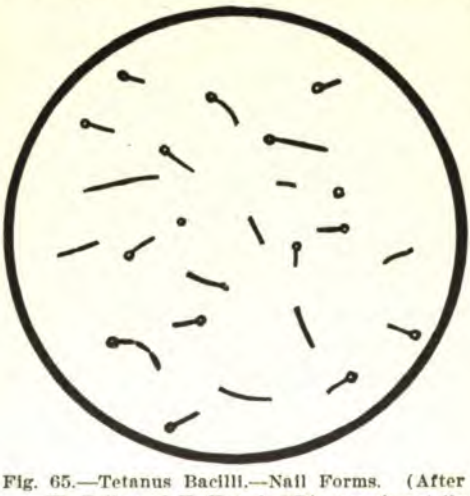

Fig. 65.—Tetanus Bacilli.—Nail Forms. (After W. Kolle and H. Hetsch, "Die experimentelle Bakteriologie, etc.," published by Urban & Schwarzenberg, Berlin.)

(*a*) *Human Tetanus*

(*Lockjaw, Trismus*)

Definition.—This is an intoxication of the nervous system with tetanus toxin, leading to tonic spasm of the muscles; it is due to infection of a wound with *B. tetani*.

Portal of Entry.—If a penetrating wound be contaminated with garden earth, manure, or street dirt, infection is liable to occur. In America, Fourth of July wounds (blank cartridges) have frequently been followed by fatal tetanus.

Diphtheria antitoxin may be contaminated with tetanus toxin and cause death, as in the lamentable experience in St. Louis (1901), when 7 children succumbed to tetanus thus caused (Bolton, Fisch, and Walden). Vaccine virus and bacterial vaccines may, if not properly controlled, be contaminated by tetanus spores. A United States law (1902) now requires that all serums and vaccines sold in interstate traffic be first tested upon animals to insure freedom from contamination. Gelatin often contains tetanus spores and human tetanus has been produced by injection of imperfectly sterilized solutions of gelatin, used as a hemostatic. Human infection is usually preceded by a known trauma (*tetanus traumaticus*). Sometimes the mode of infection is entirely unknown (*tetanus idiopathicus*). Formerly, in a few cases, it was thought to follow exposure to cold (*tetanus rheumaticus*). The two latter forms may be instances of infection by inhalation of tetanus spores, though this is not certain.

Incubation Period.—This varies from 3 to 20 days; it is usually between 4 and 10 days.

Symptoms.—The patients first notice a feeling of stiffness and tension in the masseters, and in the muscles of the face and neck. The tonic spasm of the muscles of the face gives rise to a characteristic rigid appearance resembling a smile (*risus sardonicus*). Later, the muscles of the trunk become involved and there may be marked over-extension of the back, the body being supported by the head and the heels (*opisthotonos*); or there may be rigidity of the trunk and extremities in a straight line (*orthotonos*); or spasm of the abdominal muscles so that the body is bent forward (*emprosthotonos*). External stimulation (noises, etc.) may excite a paroxysmal increase of spasm, associated with violent pain and dyspnea. There is no fever at first; later, the temperature rises, especially just before death. The mind is usually clear throughout. Constipation is marked, and defecation is painful. When the face is the portal of entry, facial paralysis occurs and there is difficulty in swallowing (*tetanus facialis, head tetanus, tetanus hydrophobicus*).

In the Southern States, especially among the poor, infection at the umbilicus in the new-born is not uncommon (*tetanus neonatorum*).

The tetanus sometimes seen in puerperal infections (*tetanus puerperalis*) is usually severe.

Course of the Disease.—In the severer forms, death occurs within 3 or 4 days after the appearance of the symptoms. If the patients live for a week, they usually recover. In the milder forms, the incubation period is longer, and all the symptoms are milder. The mortality, before the serum treatment, varied from 50 per cent to 90 per cent. Since the cam-

paign for a "safe and sane" celebration of July 4th, for the radical treatment of penetrating wounds, and for prophylactic inoculation with antitoxin, has been carried on, a great many cases of tetanus have undoubtedly been prevented.

Diagnosis.—This is usually easy from the history and the symptoms. In doubtful cases, *meningitis, strychnin poisoning,* and *rabies* should be borne in mind. Once symptoms have appeared, it is usually too late to save the patient; *the all-important thing is to prevent the development of tetanus!*

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7. Diseases Due to the Influenza Bacillus

Influenza Bacillus.—*Bacillus influenzæ* (R. Pfeiffer, 1892-3) is an extremely minute bacillus, rather irregular in length, with rounded ends, and very difficult to grow. It stains best with dilute carbol-fuchsin; it is Gram-negative, non-motile. It is aërobic, and grows best on blood-agar, on which it appears as minute, colorless, transparent colonies. Because it grows only on hemoglobin-containing media, it is classed among the "hemoglobinophil" bacilli. It is often difficult to distinguish it from similar bacilli (pseudo-influenza bacilli, bacillus of trachoma, bacillus of whooping-cough, xerosis bacilli), but the grouping in smears of purulent secretion is considered characteristic. The organisms rarely form chains, but lie in irregular thick clusters, without parallelism.

(*a*) *Influenza* (*La Grippe*)

Definition.—An infectious and highly contagious disease, due to *Bacillus influenzæ*, occurring generally in epidemics; after each epidemic it continues to appear sporadically for several years.

In the great epidemics thousands are attacked within a very brief period. Thus half the inhabitants of a district may be attacked within a few weeks. The morbidity is great, the mortality usually small.

Portal of Entry.—Usually, the bacillus enters through the respiratory tract, probably, chiefly by "droplet-infection."

Symptoms.—The incubation period is usually from 1 to 4 days. The symptoms vary according to the predominant localization of the bacilli or their toxins. The onset is usually sudden, often with chills and fever. Herpes simplex is very often present. In most cases, the attack is quickly

over. In others, it may be prolonged. Conv
and relapses are common. Four principal
guished and, in all, marked prostration and debility are prominent features.

1. *Influenza of the respiratory tract,* with rhinitis, laryngitis, tonsillitis, tracheobronchitis, paranasal sinusitis. These cases are often complicated by influenzal pneumonia and pleurisy.

2. So-called *influenzal fever* with headache, prostration, myalgias, anorexia, and depression, without catarrhal symptoms.

3. *Gastro-intestinal influenza* with high fever, anorexia, herpes, and severe diarrhea.

4. *Influenza of the central nervous system.* Several severe forms of influenzal infection of the central and peripheral nervous system occur, e. g., influenzal meningitis, influenzal encephalitis, influenzal polyneuritis, and influenzal neuralgias (persistent). Dr. B. A. Cohoe has reported a case of influenzal meningitis, from my service.

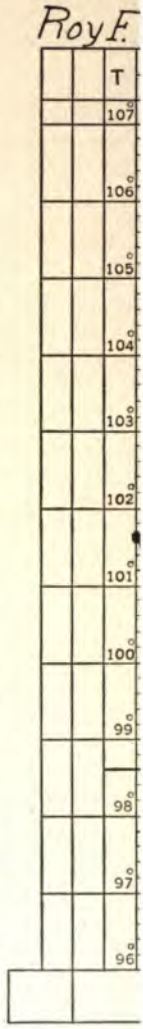

Fig. 66.–

Pure influenzal infections do not necessarily change the leukocyte count. In mixed infection with streptococci and pneumococci, leukocytosis is seen. One attack does not confer immun other attacks.

Complications.—Endocarditis, meningi thritis, conjunctivitis, and especially otitis acute process or as sequelæ.

Patients with phthisical or bronchiectat bacillus carriers, and may be responsible f

year to year when climatic conditions increase disposition in a community. F. P. Lord of Boston found influenza bacilli in the sputum in a large proportion of expectorating patients in an interepidemic period. Boggs has called attention to the presence of influenza bacilli in the sputum from bronchiectatic cavities.

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8. Diseases Due to the Bacillus of Bordet and Gengou

Bacillus of Bordet and Gengou.—This bacillus closely resembles the influenza bacillus, but is slightly larger and shows less tendency to pleomorphism. It is usually present in the sputum of whooping-cough patients, and has been cultivated on a glycerin-potato-blood-agar medium (Bordet). It is a bi-polar-staining bacillus; Bordet and Gengou believe that it is the etiological agent in whooping-cough since in their hands the serum from convalescents from whooping-cough yields a positive agglutination reaction, or more often a complement-fixation reaction, with their bacillus. Fränkel, however, could cultivate this bacillus in only 8 out of 38 cases;

moreover, serum from convalescents never agglutinated it, and complement fixation was positive in only 1 of 5 cases tested. Similar reports are made by Scheller (1912), Odaira (1911), Wollstein (1909), and Weil (1913).

Many still believe that the disease is due to the bacillus influenzæ. Czerny thinks that whooping-cough is not an etiological unity, but may be due to different infectious agents. If there is one specific agent, the whooping-cough due to it may be called "essential whooping-cough," and the other forms, "symptomatic whooping-cough." Apparently in the spasmophil diathesis, a cough like that in pertussis may occur in the absence of any specific infectious agent.

Luetscher, however, finds the Bordet-Gengou bacillus present in many cases of whooping-cough in Baltimore. According to Mallory and Horner, the bacilli are present in great numbers on the surface of the tracheal epithelium, where they mechanically paralyze the cilia. The question of the etiology of pertussis is not yet wholly satisfacorily settled.

(*a*) *Whooping-cough*

(*Pertussis, Tussis convulsiva, Fr. Coqueluche*)

Definition.—A disease directly contagious, especially in its early stages, characterized by paroxysms of coughing, often accompanied by vomiting, and occurring, usually, in epidemics among children. The cough in the convulsive stage sets in with a series of 5-30 short expiratory coughs, followed by a loud inspiratory noise (whoop). For the etiology, see above.

Susceptibility.—Among animals, dogs, cats, and monkeys are known to be susceptible. Children between 6 months and 5 years of age are extremely susceptible, but the disease may occur at any age. One attack usually yields permanent immunity.

Nature of the Disease.—According to Reyher, the pertussis syndrome may arise:

1. From an *intense stimulus*, exerted upon the respiratory mucous membrane, most often by an exogenous cause (*essential whooping-cough*). The exciting stimulus can be conditioned by (a) the production of special irritants by an infectious agent; (b) the localization of an infectious agent at a site of predilection for reflex cough (e. g., regio interarytenoidea); (c) the factors (a) and (b) together.

2. From a *heightened irritability* of the nervous system of the sick child, in which an ordinary catarrh may suffice for the production of the syndrome; here an endogenous cause plays the main rôle (*symtomatic whooping-cough*). This is observed (a) in children with spasmophil diathesis, when they contract an ordinary respiratory cough; (b) in older neuropathic persons in the same circumstances.

3. From a combination of the effect of an *intense stimulus* with a *heightened irritability*.

Symptoms.—These come on after an incubation period of, ordinarily, 3 to 8 days.

In the *catarrhal stage,* they consist of sneezing, running of the nose, headache, lacrymation, cough and slight fever, lasting 3 to 14 days.

The *convulsive stage* is characterized by an irrepressible feeling of tickling in the larynx and repeated paroxysms of coughing, each followed by a whoop. At the end of a paroxysm, viscid, glassy sputum is expectorated (or expelled by gagging or vomiting movements); on microscopic examination this sputum is characterized by the presence of large amounts of squamous epithelium, each cell stuffed full of small short bacilli. The paroxysms may be so severe as to cause asphyxia. There is often vomiting, epistaxis, conjunctival hemorrhage, and involuntary urination and defecation. After a paroxysm there is a brief period of exhaustion and sweating. The child may then resume its play and act as though it were perfectly well. A child may suffer from 10 to 15 or more attacks per day. The severer attacks occur in the night and toward morning. Paroxysms are often precipitated by emotion, crying, pharyngeal irritation, dust, etc. This convulsive stage lasts from 2 to 6 weeks; it may sometimes continue for several months. Convalescence is gradual.

In epidemics, mild and abortive cases may be seen. The white cell count in the blood is usually increased. On physical examination, signs of diffuse bronchitis, and, in severe cases, of pulmonary emphysema and of dilatation of the right heart are found.

Complications.—Capillary bronchitis; bronchopneumonia (very fatal in young children, especially if rachitic or scrofulous); emphysema; pneumothorax; apoplexy.

Sequelae.—Emphysema; pulmonary tuberculosis; tuberculous meningitis.

Diagnosis.—This is easy, as far as the clinical syndrome is concerned, in typical cases with the whoop. The diagnosis is often difficult, or impossible, in the catarrhal stage, especially when there is no history of exposure. But if we assume the existence of (1) an "essential (specific) whooping-cough," and (2) a "symptomatic (non-specific) whooping-cough," there will often be great difficulty in distinguishing the two. One may make (1) cultures for the Bordet-Gengou bacillus, and (2) serodiagnostic tests in the *later* disease or in the convalescence for agglutination and for complement fixation; but the antibodies develop too late in the disease to permit of an early serodiagnosis (Netter and Weil, 1913).

In the catarrhal stage, or in rudimentary forms, we may (1) seek a history of exposure, (2) look for a lymphocytosis, (3) look for pale urine of high specific gravity rich in uric acid; but these are not wholly satisfactory data on which to make a diagnosis!

In sucklings and in children up to 2 years of age, we should ascertain whether or not the signs of a spasmophilia (Chvostek's facial phenomenon,

increased electrical excitability of the nerves) are present. In case they are present we should be cautious in making the diagnosis of an essential or specific whooping-cough; it may be only a symptomatic whooping-cough in a spasmophilic child, due to an ordinary catarrh (Czerny); the latter diagnosis is strongly supported if there be (1) no outspoken catarrhal stages preceding the convulsive attacks, and (2) no copious excretion of mucus containing flat epithelium full of bacilli, at the end of the paroxysm.

Tuberculosis of the bronchial glands may cause similar paroxysms (röntgenogram; percussion; tuberculin test; course).

Hysterical cough may simulate whooping-cough, but there is no vomiting after the paroxysms and no preceding catarrhal stage; usually there are no paroxysms at night and other signs of hysteria are present.

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9. Diseases Due to the Plague Bacillus

Plague Bacillus.—*Bacillus pestis* usually assumes the form of a short rod, but it is often polymorphous; its ends are rounded; polar staining is visible in methylene blue preparations; it is Gram-negative. The bacillus is non-motile. It grows well on gelatin, at low temperatures, and is non-liquefying. It is pathogenic for mice, rats, and squirrels. The bacillus belongs to the hemorrhagic-septicemia group. It builds no true toxin, but injures through its endotoxins.

(*a*) *Plague*

Definition.—An infection due to *Bacillus pestis,* usually causing swelling of the nearest lymph gland (bubo); it may, however, give rise to septicemia, or to pneumonia.

Portals of Entry.—The bacillus usually enters through a minute wound (flea-bite) in the skin (axillary and inguinal buboes); occasionally, entrance is by inhalation (plague pneumonia). Epidemics in rats usually precede the larger human epidemics. Rat fleas (*Pulex cheopis*) are concerned in the transfer of the bacilli from rat to rat, and possibly also from rat to man. The *Pulex irritans* or common flea differs somewhat from the rat flea.

Fig. 67.—Pulex irritans. (After W. Braun, "Die thierischen Parasiten des Menschen," published by Bale Sons & Danielsson, London.)

When plague is epidemic, the morbidity increases from October to February and March, and then declines.

In Egypt, the small epidemics are of the bubonic type and due to infection from rats. In winter, the cases are often of the pneumonic type and the infection is direct from man to man (Gottschlich).

Incubation Period.—Two to 5 to 10 days.

Symptoms.—After a brief prodromal period (malaise, anorexia, headache, pain in back) there is usually a sudden onset with chill, violent headache and vertigo, often with nausea and vomiting, high fever, delirium. In one or two days a bubo, a plague pustule, or a plague pneumonia becomes demonstrable. As members of a Commission to the Orient (1899), Flexner and I, with Drs. Flint and Gay, had opportunity of studying the disease, clinically and at autopsy, with Lowson in Hong Kong. Later, with Flint, I saw 800 cases in one day at the Plague Hospital in Poona, near Bombay. On the average, a new patient entered the hospital every 8 minutes, and a plague cadaver was carried out every 10 minutes of the day.

In 1900, Flexner, Novy and I, as a Commission appointed by the U. S. Government, confirmed the diagnosis of the existence of plague in San Francisco, after which the admirable Campaign of Extermination was undertaken by the local authorities in coöperation with the United States Public Health Service.

The Plague Bubo.—The lymph gland nearest the portal of entry becomes large and tender (primary bubo); thence, the bacilli may enter the blood and cause general infection, with metastatic involvement, and swelling of distant lymph glands (secondary buboes). The juice aspirated from the swollen lymph glands contains enormous numbers of plague bacilli.

Plague Pustule, or Carbuncle.—This is a bluish red, painful infiltration of the skin, varying in size from that of a hemp-seed to that of a quarter, with vesicle formation; the turbid fluid contents contain enormous numbers of plague bacilli. This skin-plague is usually metastatic in origin.

Pneumonic Plague.—This is the severest form of plague and is almost uniformly fatal. The hemorrhagic sputum contains plague bacilli. Heart failure occurs early, death ensuing in from 2 to 5 days after onset of the infection. Secondary buboes are not uncommon. (Plate IV, Fig. 2.)

Diagnosis.—This is easy in epidemics. It is often difficult to recognize the first case, though this is, of course, extremely important. The bubonic form is sometimes confused with inguinal buboes due to soft chancre, or to gonorrhea. If plague be suspected, the lymph gland should be aspirated, and the juice examined bacteriologically. Smears stained in carbol-methylene-blue reveal the polar-staining bacilli; the nature of the bacillus can be confirmed by cultures and by inoculations of guinea-pigs.

Recently a plaguelike disease due to *Bacillus tularense* has been discovered by McCoy and Chapin in California, and observed by Wherry and Lamb in Ohio. The patients present an ulcerative conjunctivitis involving the palpebral conjunctivae and accompanied by enlargement of the preauricular and the cervical lymph-glands on the side affected, fever, and prostration. The disease appears to be contracted from rodents (ground-squirrels, wild rabbits), possibly through the intermediation of insects (fleas, flies).

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10. Diseases Due to the Typhoid Bacillus

Typhoid Bacillus.—*Bacillus typhosus* (Eberth-Gaffky) is a short rod with rounded ends, actively motile (peritrichous flagella), staining with ordinary dyes, but Gram-negative. It is easily grown on ordinary media, not liquefying gelatin. It can be distinguished from *B. coli* by various special cultural tests (Drigalski-Conradi medium, Endo's fuchsin-sulphite-agar, litmus milk, indol formation, etc., *q. v.*), and from *B. col*

Fig. 68.—This Map for 1907 Shows a Large Number of Cases Distributed Evenly Throughout a City. Many of These Cases Were Probably Caused by Infected Water, but it is Hard to Separate the Cases Caused by Water-borne Infection from Those Caused by Flies. (After W. R. Stokes and F. W. Hachtel, Arch. Int. Med.)

Fig. 69.—The Map for 1906 Shows a Typical Milk Epidemic, as Shown by Large Number of Black Pins in Upper Portion of Map. The Rest of the City, when Compared with the Map of 1907, Shows a Much Smaller Number of Cases. (After W. R. Stokes and F. W. Hachtel, Arch. Int. Med.)

and *B. paratyphosus* by serological reactions (agglutinin test, bacteriolysin test).

The typhoid bacillus belongs to the so-called **typhoid-colon group,** which includes also the bacillus of hog-cholera, Gärtner's bacillus, the paratyphoid bacillus, the dysentery bacillus, *Bacillus fecalis alcaligenes*, and the bacillus of mouse typhoid.

In the table following the discussion of the paratyphoid diseases, the characteristics of several of the members of the group are synoptically arranged.

(*a*) *Typhoid Fever*

(*Typhus abdominalis*)

History.—Through the careful analysis of clinical symptoms and the study of pathological anatomy, a group of fevers known as typhoid fever was gradually separated from other conditions, especially from typhus exanthematicus, relapsing fever, plague, and yellow fever. It was only after the development of etiological studies, and especially after the intro-

duction of bacteriological methods and biological immunity reactions that this "clinical typhoid fever" could be further analyzed, and divided into several distinct diseases on the ground of etiology (*B. typhosus, B. paratyphosus* A, *B. paratyphosus* B, etc.). We now speak of these, taken together, as the **typhoidal diseases,** and, among them, distinguish (1) typhus abdominalis, (2) paratyphus, and (3) typhus manchuricus.

Definition of True Typhoid Fever (Typhus abdominalis).—An infectious disease with continued fever due to the *B. typhosus,* which is always present in the blood of patients suffering from the disease; the fever lasts usually from 2 to 4 weeks. The disease is clinically characterized by a palpable spleen, rose spots, leukopenia and a pulse-temperature curve that shows a relative bradycardia. It is occasionally complicated by intestinal hemorrhage, or by perforative peritonitis. The mortality of the disease varies between 8 per cent and 12 per cent, in most epidemics.

Epidemiology.—Every case of typhoid comes from some preëxisting case, directly or indirectly. The typhoid patient gives off typhoid bacilli, chiefly through the feces, sometimes also through the urine; other people are less often infected by direct contact with the sick than by indirect transmission through polluted drinking-water, milk, or food, such pollution often being due to the so-called typhoid bacillus hosts (i. e., persons who have never had typhoid or who have had an attack and

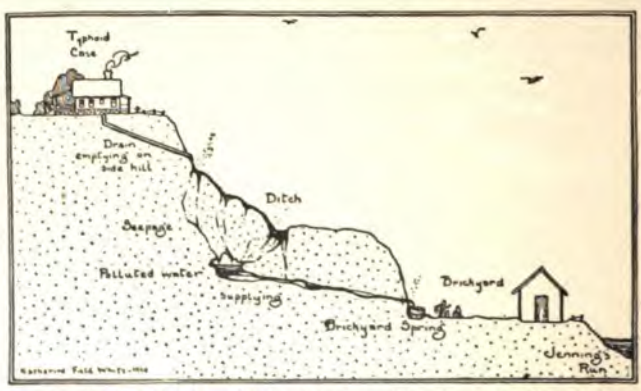

Fig. 70.—The Spring in the Brickyard Furnished an Abundant Supply of Clear Water. Following the Development of a Typhoid Case in the Cottage on the Hill, 108 of the 200 Workmen in the Brickyard Became Ill with Typhoid Fever. (After E. O. Jordan, J. Am. M. Ass.)

continue to give off from their bodies bacilli, for a shorter or longer period, thus menacing the health of people about them).

Human beings who harbor typhoid bacilli are, as we have said, spoken of as *typhoid hosts.* Among them, those who are suffering from typhoid, or who have earlier had typhoid, are called *typhoid-bacillus excretors,* while those who have never had typhoid, or at any rate are not known to have had it, are called *typhoid-bacillus carriers.* The condition of "host" may be temporary or chronic. Most chronic typhoid hosts are women,

perhaps because they more often suffer from gall-stones. Only 1 to 4 per cent of typhoid excretors become chronic typhoid hosts, though many are temporary hosts for a few months after defervescence.

Large epidemics, and those of sudden outbreak, are due nearly always either to a contaminated water supply or to a contaminated milk supply. Small epidemics may be due to contaminated foods (oysters, butter, etc.). Food may be infected either by a human typhoid host or by flies. The infection atrium in human beings is nearly always the digestive tract.

Disposition.—Age is important, the majority of the patients infected being between the 15th and the 35th year, over half the cases occurring between the 15th and 25th years. Sex is important only in as far as the exposure to infected material differs. Strong, healthy, young people are fully as often infected as feebler persons. House infection (family infection) is common (contact, common drinking-water and food). Sporadic cases of typhoid are usually due to contact infection, often from carriers.

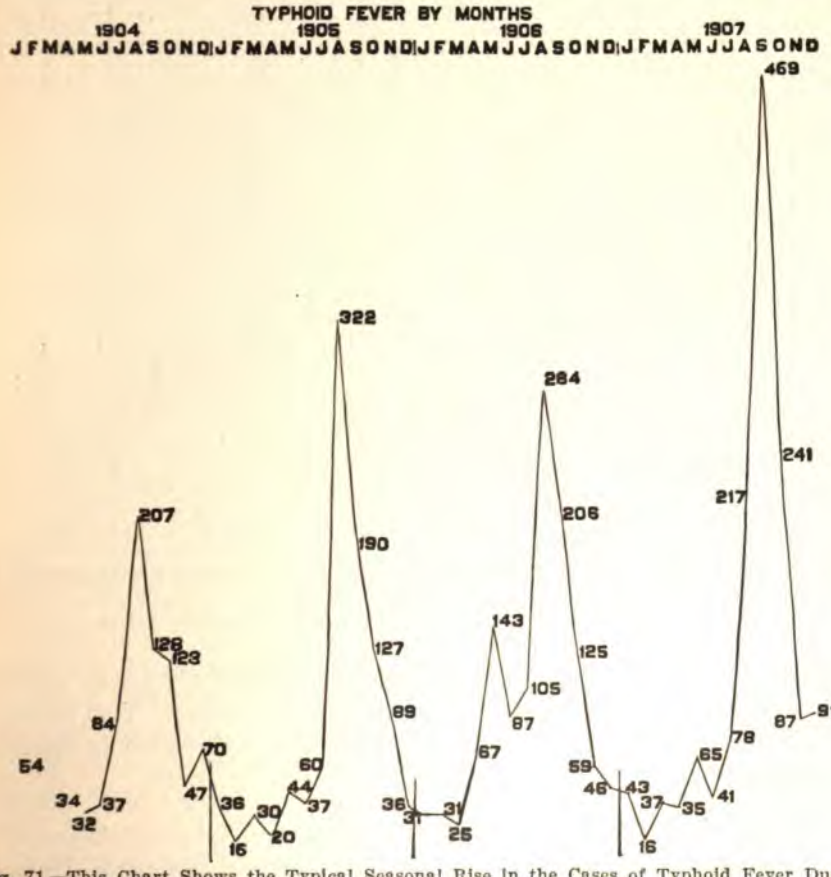

Fig. 71.—This Chart Shows the Typical Seasonal Rise in the Cases of Typhoid Fever During the Months of July, August and September When Flies are Most Prevalent. (After W. R. Stokes and F. W. Hachtel, Arch. Int. Med.)

The morbidity from typhoid fever is highest in the summer and autumn months. The cases are fewest from January to April.

Incubation Period.—This is somewhat uncertain; it is believed to be, usually, 3 or 4 days, but occasionally shorter (1 to 2 days), or longer (2 to 3 weeks).

Symptoms.—During the incubation period, certain *prodromata* may be felt—anorexia, slight headache, insomnia, malaise, bronchitis.

The patient then begins to have FEVER, which follows a characteristic course, gradually rising (*stadium incrementi*), then remaining continuous (*acme*), then becoming markedly remittent or intermittent (*amphibolous stage*), and finally ending by lysis (*defervescence*), to be followed by a few days of *subnormal temperature* in the early part of convalescence.

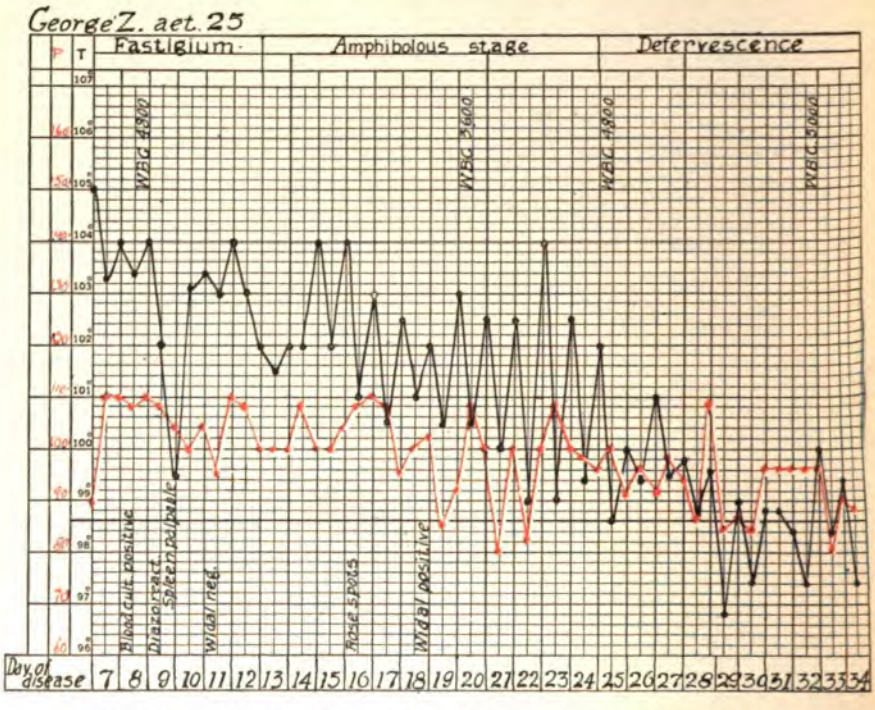

Fig. 72.—Temperature Chart of Typhoid Fever. (Personal Observation.)

It is practically convenient to classify the clinical symptoms and the pathological changes according to the *weeks of the disease*. This practice, though convenient, is purely schematic, and every physician is familiar with marked deviations from the scheme.

The Typical Course of Typhoid Fever.

FIRST WEEK (STADIUM INCREMENTI. HYPERPLASIA OF PEYER'S PATCHES).—The fever curve shows a steplike ascent, the temperature

each morning and evening being higher than that of the day before, until by the 3rd or the 5th day, it may be 104° or 105° F. Among the symptoms of the first week are: headache; pain in the back; chilly sensations; sometimes actual rigor; anorexia; disinclination for exercise; coated tongue with red edges; often epistaxis; slight abdominal distention; usually constipation, rarely diarrhea; sometimes, palpable spleen; pulse slow, con-

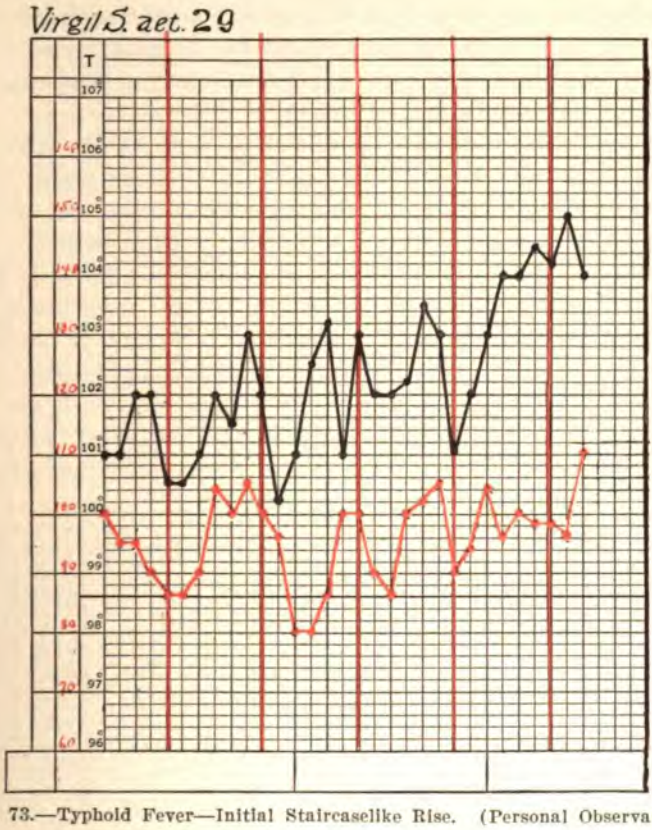

Fig. 73.—Typhoid Fever—Initial Staircaselike Rise. (Personal Observation.)

trasted with the elevation of temperature, often dicrotic; sometimes rhonchi in the lungs. The psyche may be a little dulled; there is rarely delirium at this stage (initial delirium). The skin is dry and hot. *No herpes. No coryza.* There is almost always a leukopenia (W. B. C. 3,500 to 7,000) with relative increase in the large mononuclear cells. The **blood culture** is positive for *B. typhosus* in over 90 per cent of the cases if made during the first week. The Widal test is negative at this stage. The ophthalmic reaction of Austrian is usually positive. The diazo-reaction of Ehrlich is often positive in the urine after the middle of the first week, though, if the patients drink much water, it may not appear.

Second Week (First Half of Stadium acmes. Necrosis and Sloughing of Peyer's Patches).—The temperature curve during the second week shows a continuous fever, with slight morning remissions. The pulse, in relation to height of fever, may be only slightly accelerated (a striking feature); it is usually dicrotic. All the subjective symptoms are exaggerated until the 10th day, when the headache usually stops, and the patient becomes more apathetic and dull, "typhoid state," or he may becomes restless and delirious, especially at night. In the severer cases, one may notice jumping of the tendons (*subsultus tendinum*), or a tendency to pick at the bed-clothes (*carphologia*). Involuntary urination and defecation are not uncommon in soporous patients.

From the 8th day on, **rose spots** may appear on the abdomen, the chest, and the back, coming in "crops." This typhoid roseola, when present, is very helpful for diagnosis. In neglected mouths, we see sordes on lips, teeth and tongue. The spleen, as a rule, becomes palpable. Meteorism may develop; there is gurgling in the right iliac fossa on palpation. Sometimes there are pea-soup stools (3–4); cultures from the stools yield typhoid bacilli (Drigalski-Conradi medium; Endo agar). Some of the patients are constipated. There is usually a febrile nephropathy (oliguria, albuminuria, cylindruria). A diffuse bronchitis can usually be made out on auscultation. The leukopenia continues and the blood culture is still positive, but there are fewer bacilli per cubic centimeter of blood. The

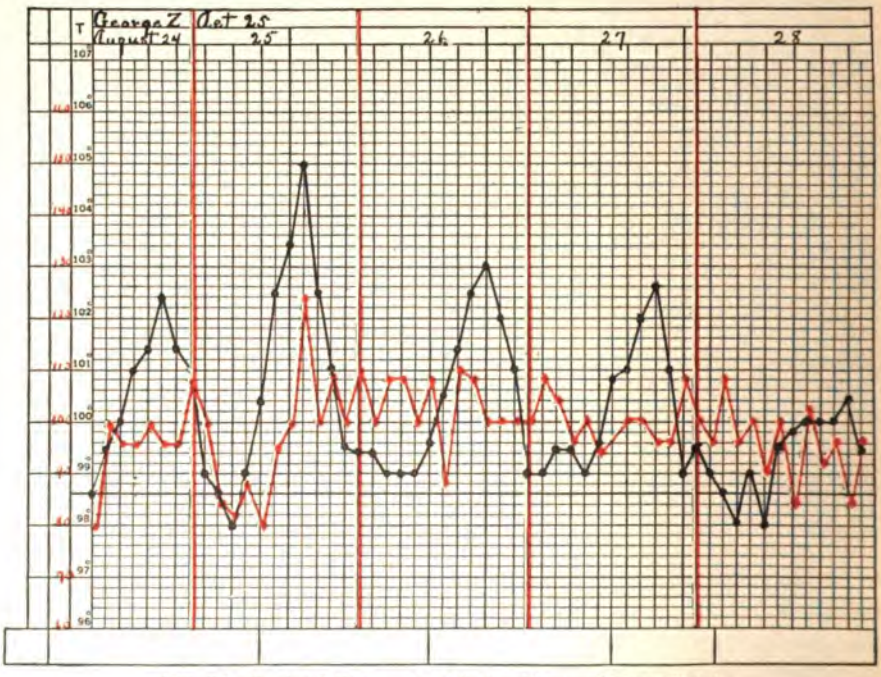

Fig. 74.—Typhoid Fever—Amphibolus Stage—2-Hour Chart.

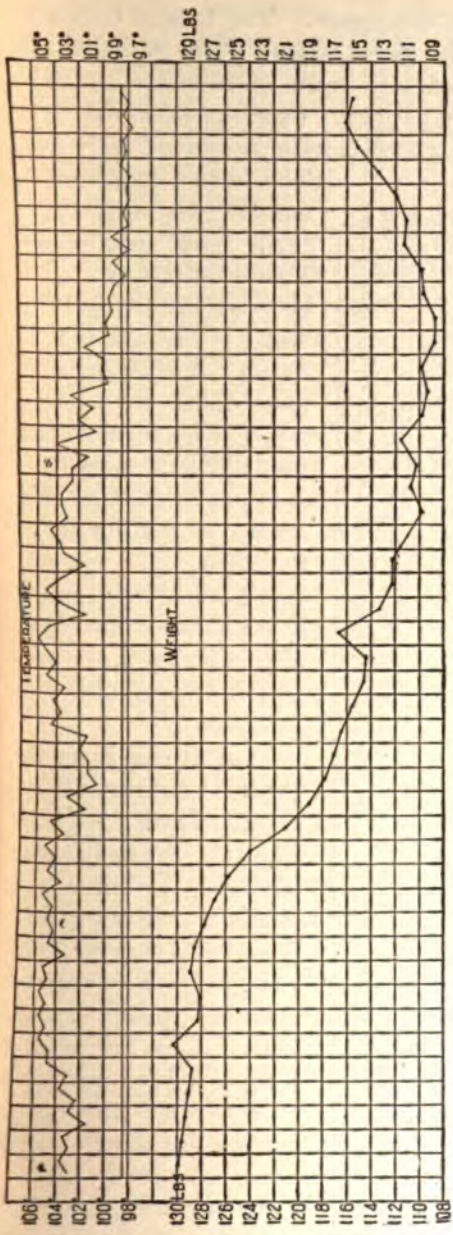

Fig. 75.—Chart Showing Loss of Weight in Typhoid Fever Despite a Food Intake Averaging 2,600 Calories per Day. (After J. Puritz from W. Coleman's Article, Am. J. M. Sc.)

Widal reaction sometimes becomes positive during the second week, though it often remains negative. **Intestinal hemorrhage** is not uncommon at this stage, due to oozing from the hyperemic, spongy Peyer's patches.

Third Week (Second Half of Stadium acmes. Continued Sloughing of Peyer's Patches, with Formation of Intestinal Ulcers).—The temperature chart may continue as a fastigium, but it now often enters upon the period of "steep curves" due to marked morning remissions and evening exacerbations (*amphibolous stage*). Toward the end of the week, the evening temperature may begin to fall and the *stadium decrementi* commences.

Intestinal hemorrhage is less common than in the second week. From this time on, the danger of **perforation** of an ulcer and of perforative peritonitis must be kept in mind. Bed-sores (decubitus) are prone to develop in the very sick, especially when the skin is neglected or in dull patients with urinary incontinence; skillful nursing will usually prevent them. Bronchopneumonia or circulatory failure may complicate the clinical picture. The mental state is often clearer than in the second week.

Fourth Week (Lytic Fall of Temperature, or Stadium decrementi. Healing of Ulcers).—The subjective symptoms now gradually disappear. The temperature falls, and the pulse becomes slower; there is often an outspoken bradycardia, though in severe cases, a slight tachycardia may develop, due to myocardial weakness. The spleen may

cease to be palpable. The meteorism disappears. The tongue begins to clean and the appetite to return. The thirst lessens. The patient looks somewhat emaciated and shows a moderate grade of secondary anemia.

Fifth Week (Subnormal Temperature. Convalescence).—The temperature now becomes subnormal, and remains so for from 6 to 8 days. The urine increases in amount; the appetite returns and usually becomes ravenous. The body weight begins to increase. The spleen is no longer palpable (except in cases liable to relapse). There is a rather marked bradycardia. Sometimes desquamation of the skin occurs, or falling out of the hair. In patients who have become greatly exhausted and emaciated, a post-typhoid psychosis may develop (exhaustion psychosis).

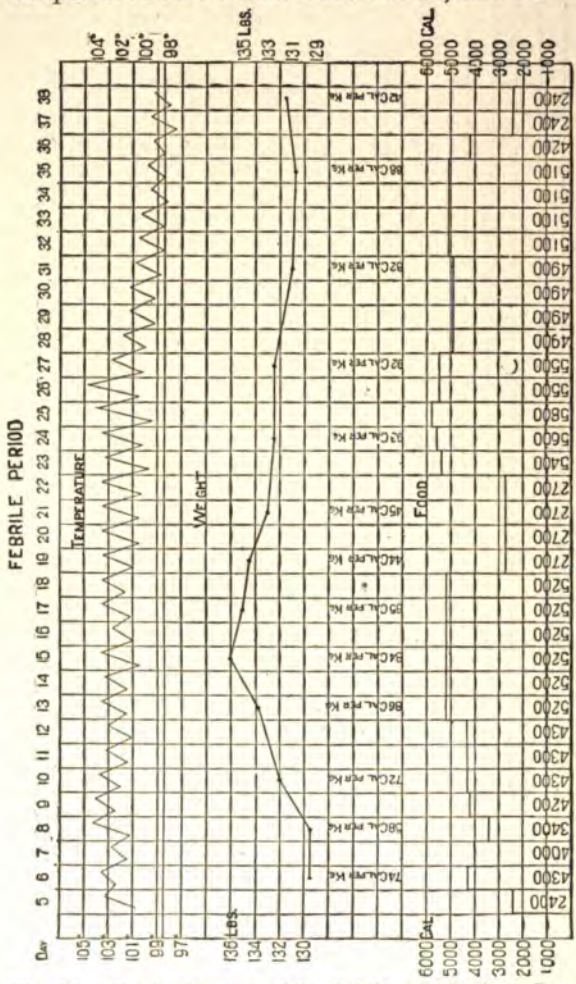

Fig. 76.—Chart Showing that Weight Equilibrium Can be Maintained by the High Calory Diet in Typhoid Fever. (After W. Coleman, Am. J. M. Sc.)

Variations from the Typical Course of Typhoid Fever. — Mild Forms.—In some cases, the fever is never high and is over in a few days (*typhus levissimus*). In a few cases, the symptoms may be severe at first, with high fever, and then quickly disappear (*typhus abortivus*). When the fall of temperature is by crisis, sporadic typhus fever, or Brill's disease may be suspected; if the blood culture be negative for *B. typhosus* and for *B. paratyphosus*, a guinea-pig should be injected and the temperature curve watched (Anderson's test for Brill's disease, q. v.) and an anaërobic culture made by Plotz's method for *B. typhi-exanthematici*.

Many patients go to bed as soon as the temperature begins to rise, but, in some, the general symptoms are so slight, or the infected are so

indiscreet, that the patients walk about (*typhus ambulatorius*) until they are surprised, perhaps, by an intestinal hemorrhage, or by the symptoms of perforative peritonitis.

Recrudescences and Relapses in Typhoid Fever.—In the stadium decrementi, the temperature, instead of continuing to fall, may rise again (*recrudescence or intercurrent relapse*), or, in the period of convalescence, after the temperature has been normal, or even subnormal for from 1 to 50 days, it may gradually rise again, the patient passing through a second usually shorter and often less severe attack (*true relapse* or *recidive*). A patient may suffer from two, three, or even more of these relapses. At the beginning of every relapse, blood cultures show a renewal of the bacillemia. Autopsies made in such cases show involvement of a new set of Peyer's patches, or of solitary follicles, with each relapse. Such relapses are often attributed

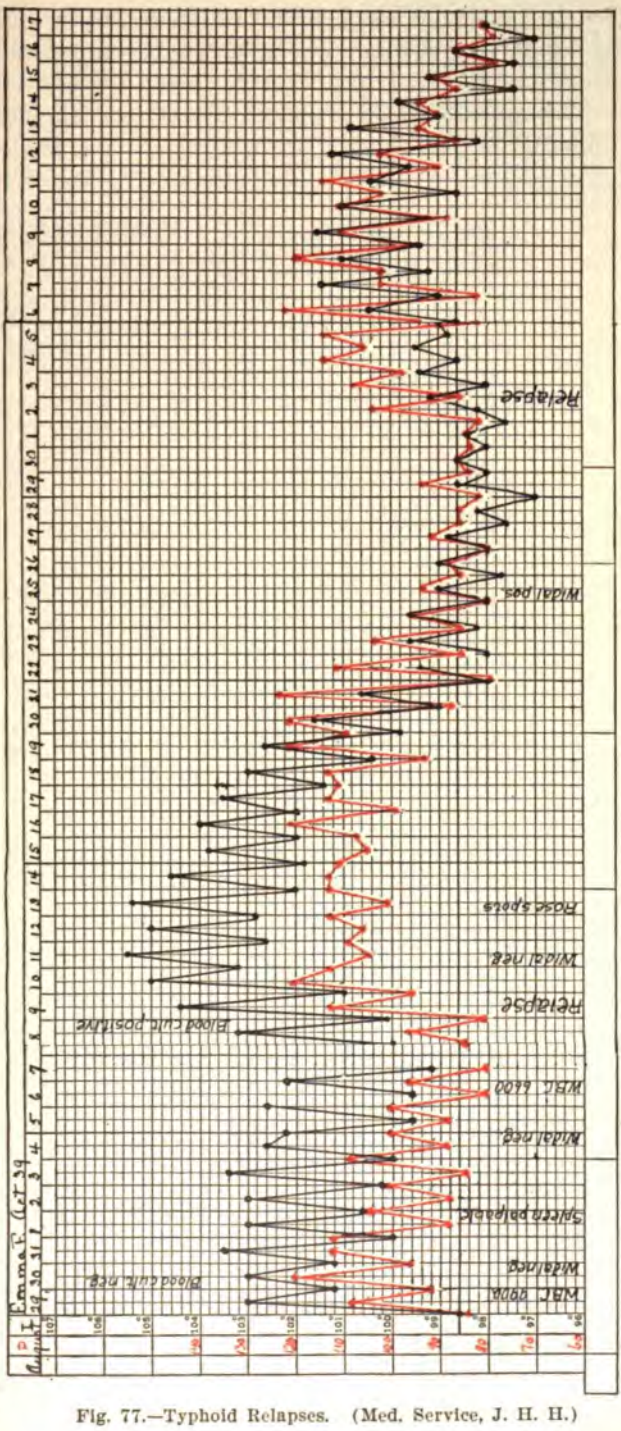

Fig. 77.—Typhoid Relapses. (Med. Service, J. H. H.)

by the patient or his friends to dietetic errors. The real cause of relapse is wholly unknown. This much is certain—the bacilli reappear in the blood and the mesenteric lymph system becomes reinfected.

Complications of Typhoid Fever.—A number of these are of great importance, especially (1) intestinal hemorrhage, (2) intestinal perforation, (3) venous thrombosis. Other complications to be kept in mind are,

Fig. 78.—Cellular Infiltration into Heart Muscle in Typhoid Fever. The Large Number of Eosinophils is Noteworthy. (After L. Hamman, Arch. Int. Med.)

(4) bronchopneumonia, (5) otitis media, (6) myocardial insufficiency, (7) pleuritis, (8) nephritis, (9) cystitis, (10) parotitis, (11) abortion (in pregnant women), (12) meningismus and, rarely, meningitis, (13) thrombosis of cerebral arteries, (14) typhoid spine, (15) cholecystitis, (16) furunculosis, and (17) peripheral neuritis.

In rare cases, the typhoid bacilli localize in the lung, kidney or meninges, and set up violent local inflammations (*pneumotyphus, nephrotyphus, meningotyphus*).

The blood-pressure often rises sharply at the time of perforation, though it may remain unchanged. A patient who complains of abdominal pain, especially of sudden pain, should be carefully watched for the signs described; should they appear, perforation has almost certainly occurred, and will be followed by increasing distention, lessened respiratory movement of the abdomen, increase of the tenderness, the rigidity and the

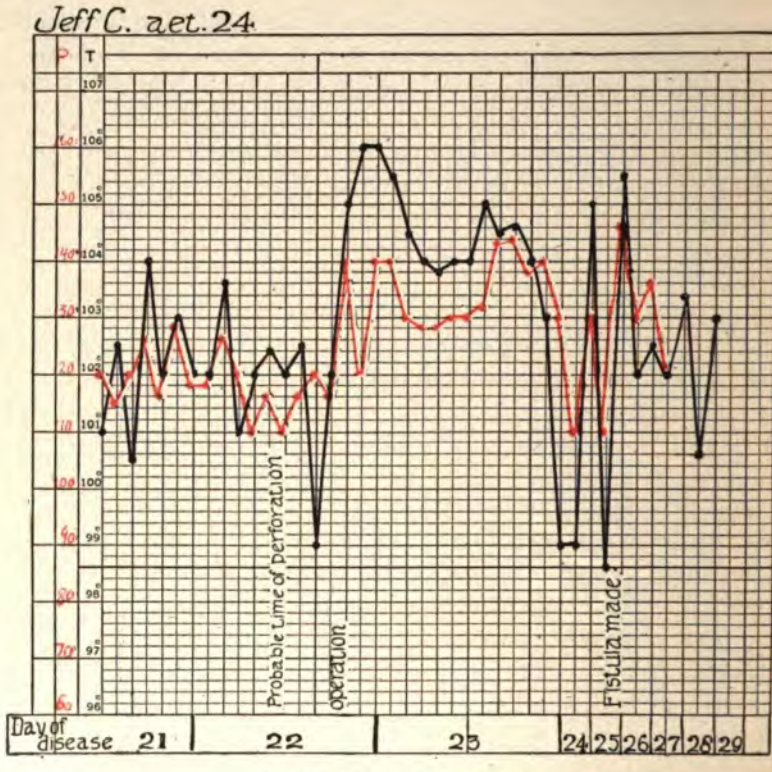

Fig. 79.—Typhoid Perforation.

muscle spasm, along with signs of free fluid in the peritoneal cavity.

The diagnosis of the condition should be made before general peritonitis develops, since if perforation has occurred, the earlier the operation is done, the greater the chance of saving the patient. Every hour counts. Two, or three, out of every five cases of perforation in typhoid fever can be saved if operation be skillfully done within a few hours after perforation has occurred. It is better in doubtful cases to operate quickly than to wait, even if now and then the abdomen be opened in the absence of perforation.

Venous Thrombosis.—This, when it occurs, most often involves the femoral vein. After complaint of pain and tenderness in Scarpa's triangle, the pulse becomes accelerated, the lower extremity begins to swell,

lood begins to increase. The swelling of
m 4 to 6 weeks, after which it gradually
tendency to edema of the leg ever after.
thrombosed. Lewis Conner has called
ulmonary infarction in cases of typhoid

ese have been referred to above. For a
ills, (2) the skin complications, and (3)
, the articles of McCrae and of Cursch-
ewis Conner's article will be found an ex-
post-typhoidal elevations of *temperature*

—This is usually easy before the end of
first week, if the following points be kept

slow in relation to the elevation of the
leukopenia; (4) absence of coryza, and of
the blood; (5) blood culture in Conradi's
tion, as modified by Austrian.

the importance of the blood culture for
ver. Any physician can draw blood, asep-
d of the elbow, and place some of it in a
should then be sent to a bacteriological
dy. A positive result can be obtained in
from 16 to 24 hours.

ct that **the Widal reaction is of very lit-**
of typhoid fever, though it may be very
tful diagnosis in which the blood culture
week, the occurrence of *typical rose spots*

tain febrile diseases, without positive
ng, may closely resemble typhoid fever.

(leukocytosis; herpes; röntgenogram;

(blood culture negative for *B. typhosus;*

tosis; blood culture negative for typhoid). A *meningismus in typhoid* frequently simulates meningitis.

5. From *typhus exanthematicus* or *Brill's disease* (blood culture; tachycardia; eruption; Anderson's guinea-pig test, q. v.).

6. From *relapsing fever* (spirochetes in stained blood-smear; temperature chart).

7. From the different varieties of *malaria* (parasites in the blood; blood culture negative).

8. From *secondary syphilis* (negative blood culture; positive Wassermann; remains of chancre).

9. From *trichinosis* (negative blood culture; outspoken eosinophilia; histology of excised muscle; history of eating raw ham or sausage).

10. From *influenza* (herpes; often coryza; negative blood culture).

11. From *ulcerative endocarditis* (cocci in blood culture; leukocytosis; heart murmurs; conjunctival petechiæ).

Prophylaxis of Typhoid Fever.—The secret in prophylaxis is to remember that the *source of all new typhoid infections* (in the last analysis) *is the infected human being* (R. Koch). The early diagnosis of typhoid cases, the disinfection of excreta, the bacteriological control of typhoid hosts, including the bacillus carriers, the protection of the water, the milk, and the food supply, the avoidance of infection by direct contact (fingers!), and the campaign against flies, are important measures.

Typhoid Hosts.—The healthy carrier presents a difficult problem. A reasonable man may, if he be a chronic host, be led to disinfect his feces and his urine, but the majority of carriers can scarcely be induced or forced to take such precautions. It is impracticable to isolate all carriers, but care should be taken to see to it that they engage in occupations that have nothing to do with the preparation, or transport, of foods, milk, or drinking-water. It was hoped that extirpation of the gall-bladder would cure the chronic carrier, but the results of operation have been unsatisfactory. *No cure for the carrier has yet been devised.* Most chronic hosts yield a positive Widal reaction!

(a) (b)

Fig. 80.—Results of Typhoid Inoculation. (a) Jacksonville, Fla., 1898, Seventh Army Corps, U. S. Army, 10,759 Men, None Given Typhoid Vaccine. (b) U. S. Army, San Antonio, Tex., 12,801 Men, All Given Typhoid Vaccine. (After E. O. Jordan—copied from Washington State Board of Health Bulletin, May, 1912, in J. Am. M. Ass.)

Preventive Inoculation.—The experience in South Africa during the Boer War, and the

erience of the United States Army during the recent mobilization on Mexican border, prove conclusively the value of preventive inocula- n against typhoid. Three successive injections of the dead bacilli, in table numbers, protect for 1-2-3 years or longer. The work of Major F. Russell of the United States Army in connection with prophylactic cination has been notable.

(*b*) *Gastroenteritis Due to Bacillus typhosus* (*Gastroenteritis typhosa*)

In rare instances, the typhoid bacillus, instead of causing typhoid fever, s rise to an acute gastroenteritis of sudden onset, with vomiting and ent diarrhea, abdominal pain, and fever, lasting two or three days. The hoid bacillus can be grown from the feces. A few bacilli may get over the blood, and the serum later agglutinates the typhoid bacillus. Here have to deal with a wholly different disease from typhoid fever; in roenteritis typhosa, it is the *surface* of the intestinal mucous mem- ne which is attacked, as in Asiatic cholera, while in true typhoid fever the *mesenteric lymph paths* and the *lymphatic tissue of Peyer's patches the solitary follicles* that are predominantly involved.

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11. Diseases Due to B. paratyphosus

Paratyphoid Bacilli.—The *Bacillus paratyphosus* has been studied carefully by Schottmüller, and by Kayser. There are two forms, the *Bacillus paratyphosus A* (or *acidumfaciens*), and the *Bacillus paratyphosus B* (or *alkalifaciens*). Of these two, the second is much the more important as the cause of disease in human beings, though either may be concerned.

Each of them is capable of setting up a disease that clinically (aside from bacteriological examinations) is indistinguishable from ordinary typhoid fever, but the same organism is capable of causing, in addition to a disease like clinical typhoid fever, any one of several local diseases in the body, viz.: (1) gastroenteritis paratyphosa, (2) pyelitis paratyphosa, (3) endometritis paratyphosa, (4) cholecystitis paratyphosa, and (5) meningitis paratyphosa. The cases may occur sporadically, or in epidemics. The infections with paratyphoid bacilli are far less numerous than cases of infection with the *B. typhosus*.

(*a*) *Gastroenteritis paratyphosa B* (*Cholera nostras paratyphosa*)

It turns out that a gastro-intestinal form of meat-poisoning, or food-poisoning, is often due to the local action of paratyphoid bacilli, especially of variety *B* upon the mucous membrane of the stomach and intestine.

Symptoms.—The onset is sudden, with violent abdominal pain. There are frequent stools for one or two days, after which there may be constipation. The fever is, as a rule, not high. Sometimes nausea and vomiting accompany the attack. Recovery usually follows in a few days. In severer cases of summer diarrhea (*cholera nostras*), the symptoms may last longer. Herpes and rose spots may appear. In fatal cases, delirium and convulsions are not uncommon. Cramps in the calves of the legs may occur. There is outspoken thirst.

Diagnosis.—The clinical picture indicates the presence of a gastroenteritis. The demonstration of the causal agent depends upon cultures from the stools (smears on Endo's agar, on Drigalski-Conradi medium, or on malachite-green-agar), with subsequent identification of the bacillus through fermentation tests and by agglutinative or bacteriologic tests with a known immune serum (q. v.).

(*b*) *Paratyphus abdominalis B*

(*Typhoid Form of Meat-, or Food-poisoning*)

Here, clinically, the picture is that of ordinary typhoid fever. The fever is usually milder, however, rarely remaining continuous for more than a short time; the average duration is briefer (21 days). The rose spots are indistinguishable from those of typhoid. Herpes occurs in 50 per cent of the cases (in marked contrast with typhoid). Intestinal hemor-

rhage is much rarer than in typhoid. Perforation occasionally occurs. The spleen is enlarged. The pulse is dicrotic and relatively infrequent, as in typhoid, and there is leukopenia with relative lymphocytosis. The agglutination titer of the serum is usually higher for *Bacillus paratyphosus B* than for *Bacillus typhosus*. The *Bacillus paratyphosus B* can be obtained by blood culture, early in the disease. Relapses are less common than in typhoid, though they sometimes occur.

Most patients recover. In fatal cases, the intestinal lesions may resemble those of typhoid, but thus far only a few autopsies are on record; sometimes there are no lesions in Peyer's patches, as in Longcope's case.

Diagnosis.—A clinical picture resembling that of typhoid fever, but beginning with a chill and associated with diarrhea, abdominal pain and herpes, speaks for paratyphoid. The exact diagnosis depends upon the demonstration of the *B. paratyphosus* in the blood culture, and of specific agglutinins and other immune bodies in the serum, later on.

(*c*) *Gastroenteritis paratyphosa A and Paratyphus abdominalis A*

This organism, also, can cause (1) a disease resembling typhoid fever (*parathyphus abdominalis A*), and also (2) a gastroenteritis (*gastroenteritis paratyphosa A*).

(*d*) *Typhus manchuricus*

Comparatively recently, Russian physicians have studied the typhoid fever of Manchuria (*typhus manchuricus*). The blood contains a bacillus belonging to the typhoid-paratyphoid group. Whether it is a bacillus already known, or a new variety, has yet to be determined.

A table based upon Schottmüller's findings and contrasting the morphological and cultural properties of bacteria of the typhoid-colon group is here appended. (See next page.)

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TYPHOID-COLON GROUP OF BACILLI. (ALL GRAM-NEGATIVE)

	B. coli	*B. typhosus*	*B. paratyphosus A*	*B. paratyphosus B. + B. enteritidis* (Gaertner)	*B. dysenteriae* (Shiga)	*B. dysenteriae* (Flexner)	*B. faecalis alcaligenes*
Motility	+	+ +	+ +	+ +	○	○	+
Flagella	+	+	+	○ +	○	○	+ Polar
Indol production	+	○	○	○	○	+ (In 2 weeks)	○
Milk coagulation	+	○	○	○	○	○	○
Litmus milk	Marked reddening	Slight reddening	Moderate reddening	At first reddening; later blue	Very slight reddening	Slight reddening	Blue
Gas production in glucose agar	+ +	○	+	+	○	○	○
Gas production in lactose agar	+ +	○	○	○	○	○	○
Drigalski-Conradi medium	Red	Blue	Blue	Blue	Blue	Blue	Blue
Endo's fuchsin agar	Very red	Colorless	Colorless	Colorless	Colorless	Colorless	Red
Malachite green agar	Inhibited	Good growth	Good growth	Good growth	Delicate growth	Delicate growth	Inhibited
Potato culture	Juicy, greyish brown	Delicate, scarcely visible	Delicate, like typhoid	Strong, like colon	Delicate, like typhoid	Delicate, like typhoid	Greyish brown

13. Diseases Due to the Dysentery Bacillus

Dysentery Bacillus.—The *Bacillus dysenteriæ* is met with in several forms (type Shiga, type Flexner, type Strong, type Y or His, etc.). The differential characters are shown in the table given on page 250.

(*a*) *Bacillary Dysentery* (*Epidemic Dysentery*)

Definition.—This is an infectious inflammation of the large intestine, and is accompanied by diarrhea, with blood, mucus, and dysentery bacilli in the stools. The disease is not accompanied by a bacteriemia as a rule, though occasionally the bacillus can be isolated from the blood as well as from the stools; the bacilli are localized in the intestinal mucous membrane and in the mesenteric lymph glands whence the toxins pass to the blood and give rise to a general intoxication.

The different types of dysentery bacilli are best distinguished, according to Lentz, by growth on 3 forms of litmus agar (mannite, maltose, saccharose). Agglutination tests with immune sera are also helpful.

Epidemiology.—Like typhoid, cases of epidemic dysentery arise from some sick individual, directly or indirectly. Fingers and flies play a rôle in the contamination. Mild infections, in ambulant patients, are especially dangerous to other individuals. Healthy *bacillus carriers* are often observed, and have been proven to be the starting point of epidemics in recent years. Direct contact infection is more common than infection by polluted water, though water, milk, and foods are sometimes a source. The disease prevails in the summer months, and is especially common among large aggregations of people (army camps, festivals, etc.).

Symptoms.—An acute and a chronic form of epidemic dysentery occur. In the ACUTE FORM the onset is insidious (digestive disturbances) after an incubation period of a few days. There is anorexia, coated tongue, tendency to diarrhea, and to colicky pains in the abdomen. After two or three days, the abdominal pains become more severe, the diarrhea becomes worse (8-30-100 stools per day). The *feces,* at first soft, like those of simple diarrhea, undergo a change, and come to consist of pure mucus, or of blood-stained mucus. There is burning and pain in the rectum on defecation (*tenesmus*). The feces are not foul, but they have a stale odor. The patients emaciate rapidly, the eyes become sunken, and the voice grows feeble; the tongue is dry and coated; the abdomen is retracted and tender on pressure; the urine is scanty; and there is slight elevation of temperature; sometimes, however, the temperature is subnormal.

The majority of patients begin to recover after 1 to 3 weeks; the stools regain their fecal consistency, the number lessens, and the appetite and

strength begin to return. **Relapses** are common (dietetic errors, cold drinks). In severer cases, death occurs at the end of 2 or 3 weeks.

Complications.—Polyarthritis; peripheral neuritis; conjunctivitis. Liver abscess is rare (contrast with amebic dysentery).

In the severer cases, type Shiga is usually found, in the milder cases, type Flexner, or type Y. The mortality in the severer forms amounts to from 10 to 15 per cent; in the milder forms it may be only 0.5 per cent (Jochmann).

In the CHRONIC FORM OF BACILLARY DYSENTERY there is emaciation, anemia, and weakness; the bowels are irregular; recurring abdominal pains are complained of; the stools contain small masses of blood-stained mucus, crowded with dysentery bacilli. In this form, the disease may continue for months or years. Many patients are unaware of the infection, and thus form the starting point of epidemics.

Diagnosis of Bacillary Dysentery.—The clinical diagnosis of dysentery is easy: diarrhea; tenesmus; blood and mucus in the stools. Microscopic examination of the feces rules out amebic dysentery. Cultures, from washed mucus, on litmus-lactose agar, and on litmus-mannite agar, followed by agglutination tests, reveal the bacillus and its type.

Amebic Dysentery is described further on.

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14. Diseases Due to the Bacillus of Ducrey

Ducrey's Bacillus.—The *bacillus of soft chancre* (Unna-Ducrey) is Gram-negative, non-motile, fairly thick bacillus, with rounded ends; is often seen in chains. It stains well with methylene blue (polar staining). It grows well on blood agar, and is pathogenic for man and monkeys reproducing soft chancre (*ulcus molle*). Smears from a soft chancre, from the juice of a bubo secondary thereto, contain large numbers of t bacilli.

(*a*) *Soft Chancre* (*Ulcus molle*)

This lesion may be single or multiple. It appears within a few da after exposure (coitus). An ulcer, with sharp margins, secreting pu soon forms. Under treatment, it usually heals quickly; neglected, it las longer, and often causes suppurative metastases (unilateral, or bilateral in the inguinal lymph glands (*suppurative bubo*). Soft chancre ma multiply locally, by auto-inoculation.

Sites.—Frenulum præputii, sulcus coronarius, and glans; also, i females, at the introitus vaginæ.

Nature.—The disease has nothing to do with syphilis, but occasionally syphilitic infection (with *Treponema pallidum*) is contracted at the sam exposure, and the sore, beginning as a soft chancre, later (3 weeks) unde goes hardening, due to the initial sclerosis of a hard chancre (*chancr mixte* of the French).

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15. Diseases Due to the Diphtheria Bacillus

Diphtheria Bacillus.—The *Bacillus diphtheriæ* (Klebs-Loeffler) is slender, non-motile, often somewhat curved bacillus, slightly swollen at t ends, and of very variable morphology. One often sees these bacilli pairs, more or less parallel to one another, and occasionally in thre *Involution forms* (clubs, dumb-bells, spindles), staining irregular Loeffler's alkaline methylene blue, are common. Diphtheria bacilli with ordinary anilin dyes best with Loeffler's blue. (Plate IV, F They are Gram-positive.

Cultures on Loeffler's serum, 6 to 20 hours old, stained by the of M. Neisser, show fine points at the ends of the bacilli—the s *Babes-Ernst polar bodies.*

NEISSER'S METHOD OF STAINING POLAR BODIES.—1. Smears are stained 1 second in a mixture of 2 parts of Solution A and 1 part of Solution B.

Solution A: Methylene blue (Höchst) 1.0.
Absolute alcohol 20.0.
Distilled water 1000.
Glacial acetic acid 50.0.

Solution B: Crystal violet (Höchst) 1.0.
Absolute alcohol 10.0.
Distilled water 300.0.

2. Wash with water.

3. Counterstain in chrysoidin solution (1 part of dye, dissolved in 300 parts hot water and filtered) for 3 seconds.

4. Wash with water.

The bodies of the bacilli are stained brown, while at each pole a minute blue granule is visible (Plate IV, Fig. 5). The bacilli resembling *B. diphtheriæ* do not show these granules.

CULTURES OF B. DIPHTHERIÆ.—The diphtheria bacillus grows best on Loeffler's blood serum in tubes or Petri dishes, at the body temperature, or a little lower.

Special nutrient media like Deycke's alkali-albuminate agar, or Tochtermann's serum agar, yield good growths, but are unnecessary.

On Loeffler's blood serum (3 parts blood serum, 1 part peptone bouillon, with 2 per cent glucose) the diphtheria bacilli grow somewhat more luxuriantly than do pseudodiphtheria bacilli or xerosis bacilli. Glycerin-ascites agar is an excellent medium, if Loeffler's blood serum be not available.

Pathogenicity.—Inoculated into the trachea of rabbits and pigeons, pseudomembranes are produced and fatal intoxications may follow. Pure cultures of the bacilli yield **diphtheria toxin**, which, injected into animals, causes intoxication and death. If sublethal doses be injected at intervals, a specific **diphtheria antitoxin** is formed. Applying this principle, enormous amounts of diphtheria antitoxin (Behring) are now prepared, in horses, and used in the treatment of diphtheria (*passive immunization*).

Genuine diphtheria bacilli can be distinguished from the xerosis bacilli of the conjunctiva, and from the pseudodiphtheria bacilli sometimes met with in the mouth or nasal cavity, in that the true diphtheria bacilli (1) in bouillon culture, give rise first to acid production, and later to a strong alkaline reaction; (2) are virulent for guinea-pigs, but, when mixed with diphtheria antitoxin before injection, lose this virulence; (3) kill animals on injection, while the others do not.

...tions.—In diphtheria infections, besides the diphtheria ... often present also streptococci, staphylococci or pneumo... (*...fections*), of great importance clinically, since the antitoxin ... the toxin produced by the *B. diphtheriæ*.

... any healthy individuals harbor diphtheria bacilli (*bacillus* ... bacilli are sometimes virulent, sometimes avirulent;

in the former instance, they are probably of importance in the starting of epidemics (Moss and Guthrie).

Forms of Diphtheria.—In human beings, the diphtheria bacillus may cause (1) a pharyngeal diphtheria, (2) a nasal diphtheria, or (3) a laryngeal diphtheria; more rarely, it sets up (4) a cutaneous diphtheria, (5) a conjunctival diphtheria, (6) a vulval diphtheria, or (7) a wound-infection diphtheria. In all instances, the incubation period seems to vary (2 to 8 days).

Susceptibility to Diphtheria.—It has recently been shown that the blood of many normal individuals contains diphtheria antitoxin, in demonstrable quantities. Thus some 80 per cent of the newborn, 90 per cent of adults, and 50 to 60 per cent of children are so protected. Such individuals are not susceptible to diphtheritic infection, and in cases of epidemics, or in instances of single exposure, the prophylactic injection of diphtheria antitoxin ordinarily given may be omitted. This new knowledge has resulted from the introduction of the *intracutaneous test of Schick.*

SCHICK'S TEST.—1/50 of the minimum lethal dose of diphtheria toxin for the guinea-pig is diluted to make 0.1 c.c. of fluid. This is injected intracutaneously, and the site of injection examined at the end of 24 hours. Those who are susceptible to diphtheritic infection show a definite inflammatory reaction. Those who are insusceptible, owing to the presence of diphtheria antitoxin in the blood, show no inflammatory reaction. (See the work of W. H. Park and his colleagues in New York, with this test.) The simple outfit devised by A. Zingher for the test will be found convenient by practitioners.

(*a*) *Pharyngeal Diphtheria*

This is the commonest form of diphtheritic infection. The bacilli multiply on the mucous membrane, and in its superficial layers, causing extensive necrosis, with formation of fibrinous membranes. Though a few bacilli may get over into the blood, the general phenomena are due to the toxins produced by the bacilli *in loco,* rather than to a bacillemia.

In the *membranous form*, a grayish white deposit is seen on the uvula, the soft palate, and tonsils (unilateral or bilateral).

In the *lacunar form*, there is redness and swelling of the uvula, soft palate, and tonsils, but no visible membrane except whitish plugs in the fossulæ (crypts) of the tonsils. These cases are often mistaken for streptococcus angina.

In the severer forms of diphtheria, black areas may appear in the membrane (*gangrenous form*), or the membrane formation may extend from the throat upward to the nose, or downward to the larynx, trachea, and bronchi (*progressive* or *spreading form*).

Symptoms.—The onset may be insidious, with fever, malaise, headache, sore throat, and foul breath. The pulse and the respiration are accelerated. Children, when infected, are apt to be dull and sleepy. If the

PLATE IV

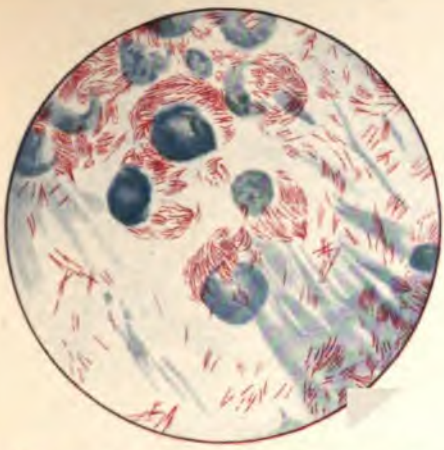

Fig. 1.—Smear from Nasal Secretion in Leprosy. (After C. Mense, "Handb. d. Tropenkrankh.," published by J. A. Barth, Leipzig.)

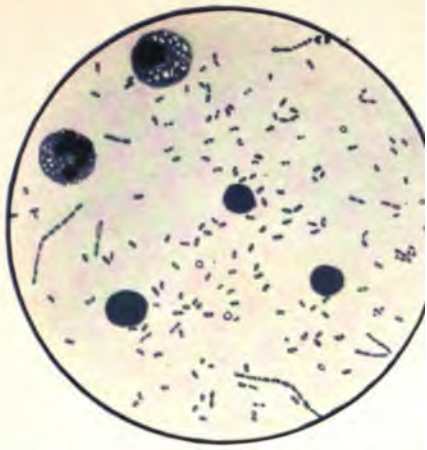

Fig. 2.—Smear from Sputum in Primary Plague-pneumonia. (After C. Mense "Handb. d. Tropenkrankh.," published by J. A. Barth, Leipzig.)

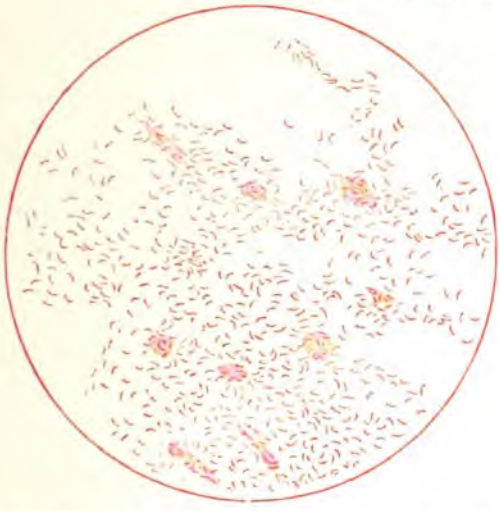

Fig. 3.—Cholera Bacillus, Pure Culture Stained with Carbolfuchsin. After L. Mohr u. R. Stachelin, "Handb. d. inner. Med.," published by J. Springer, Berlin.)

Fig. 4.—Bacillus diphtheriae—36-Hour Pure Culture. (After P. Krause, "Lehrb. d. klin. Diagnostik d. inner Krankh.," published by G. Fischer, Jena.)

Fig. 5.—Bacillus diphtheriae—Pure Culture—Neisser's Stain. (After P. Krause, "Lehrb. d. klin. Diagnostik d. inner. Krankh.," published by G. Fischer, Jena.)

condition be recognized early (inspection, throat culture), and antitoxin be given promptly, the membrane disappears in a day or two, the temperature becomes normal, and, in a week, the patient is usually well. If antitoxin be not given, the membrane spreads, the lymph glands at the angle of the jaw become large and tender, the tachycardia and fever persist, and albuminuria appears. Many of the patients, without antitoxin, die; others, after a week or two, gradually recover, though in convalescence postdiphtheritic paralyses or death from heart failure may occur. In all cases there is a leukocytosis.

(*b*) *Nasal Diphtheria*

This may occur as a primary infection, or it may be secondary, through extension of diphtheria of the throat. The nose is obstructed and a thin bloody discharge runs down over the upper lip. On rhinoscopic examination, the membrane is visible, and diphtheria bacilli are demonstrable in smears and in cultures.

(*c*) *Laryngeal Diphtheria*

This, too, may be primary, though it is more often secondary to pharyngeal, or to nasal, diphtheria. The primary cases are frequently overlooked by physicians until it is too late to save the patient.

The child is, at first, a little hoarse, and has a croupy cough, with slight fever; nothing more malign than simple "croup" may be suspected! Later, signs of laryngeal stenosis appear, with long-drawn-out, noisy inspiration, and retraction in the jugular fossa and in the epigastrium. In such cases, unless intubation, or tracheotomy, is promptly resorted to, the issue is nearly always fatal. I have, however, known patients, given up as hopeless, to expectorate a cast of the larynx and trachea, and go on to recovery.

(*d*) *Cutaneous Diphtheria*

This is due, usually, to infection of a scratch, or of a minute skin lesion (rhagades, intertrigonous eczema); it is most often seen in the groin, or about the anus. It may or may not be associated with pharyngeal diphtheria. Irregular ulcers appear, covered by a diphtheritic membrane, containing the bacilli. The condition may be confused with infantile ecthyma, or with a drug dermatosis (iodids, bromids).

(*e*) *Vulval Diphtheria*

This is usually a puerperal infection; rarely it may follow other traumata. The membrane may extend to the vagina, and may even involve the whole extent of the vaginal cavity.

(*f*) *Conjunctival Diphtheria*

Diphtheria of the conjunctiva is rare; it is usually an extension from the nose, though it may occasionally occur as a primary infection. Enlargement of the lymph glands in front of the ear quickly follows, and slight fever develops. If neglected, the eye may be lost.

Complications and Sequelæ of Diphtheria

The most important are (1) acute nephritis, (2) heart failure, (3) postdiphtheritic paralyses. In addition, (4) otitis media, (5) bronchopneumonia, or (6) polyarthritis may occur.

Nephropathies.—Though most diphtheritic patients show albuminuria and a few casts, a few have an outspoken acute nephropathy, which not infrequently goes over into chronic renal disease.

Cardiopathies.—Sudden heart failure after diphtheria is not uncommon and is greatly feared as a complication (myocardial degeneration?). It may appear early in the disease, but is more often met with in the second or the third week.

A child, apparently almost well, may, on sitting up, drop back dead. In some cases, symptoms of severe myocardial insufficiency appear (dilatation, feeble sounds, tachycardia or bradycardia, gallop rhythm); many of these patients die, but a few recover. Occasionally a partial heart block is observed.

Neuropathies.—Postdiphtheritic *paralyses* may appear, in 1-3-6 weeks after the infection. Most often the *soft palate* is paralyzed (nasal voice; regurgitation of fluids through the nose). If this occur early, it is usually due to the local inflammation; later cases are due to nerve degeneration.

Another common form is postdiphtheritic paralysis of the M. ciliaris (*accommodation paralysis*). Children find that they cannot read, and may be punished in school therefor. In a few instances, a *multiple neuritis* occurs with eye muscle paralysis, along with weakness of the arms and legs, with ataxia. Sensation is usually but little affected. The paralyses may occur, even when antitoxin has been used. The patients recover as a rule, though the disability may be prolonged.

Diagnosis of Diphtheria

The *membranous cases* of pharyngeal diphtheria can usually be recognized at once by inspection, though streptococcus anginas are occasionally accompanied by membrane formation. The *lacunar cases* can only be distinguished with certainty, by bacteriological examination. On account of the danger of overlooking a diphtheritic angina, it is a good rule to make a smear preparation, and a culture on Loeffler's serum, in every case of sore throat. The utensils for the purpose can be obtained at any corner drug store, and if the physician does not care to make the examination

himself, he may send the materials to the laboratory of the Board of Health and receive a telephonic report within 20 hours. In outspoken cases, the report need not be awaited before giving antitoxin.

Differential Diagnosis.—The pharyngeal form of diphtheria must be distinguished (by smears and cultures) from other forms of angina (*streptococcus angina, Plaut-Vincent's angina, syphilitic angina, angina scarlatinosa*).

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16. Diseases Due to the Bacillus pyocyaneus

Bacillus pyocyaneus.—The *Bacillus pyocyaneus* is a slender motile rod with a flagellum at one end. It is Gram-negative. In cultures, it liquefies gelatin; grows, in the presence of oxygen, with a greenish fluorescence on agar; and coagulates milk. It produces a proteolytic ferment (*pyocyanase*) and a soluble *toxin*. It is pathogenic for guinea-pigs.

Human Infections.—In 1897, I described a series of human infections due to this bacillus. In America, Blumer has also studied these infections, while in Europe they have been met with by many observers.

Most often, this "bacillus of green pus" is seen in mixed infections along with the pyogenic cocci, but it is entirely capable of setting up pathological processes by itself. It usually causes *local inflammations*, especially of the alimentary tract (esophagus, intestine), of the umbilicus in the new-born, of the pelvis of the kidney, etc. A *general pyocyaneus sepsis* is also known, associated with high fever, diarrhea, and a hemorrhagic or pustulo-hemorrhagic exanthem; sometimes there is also an endocarditis.

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17. Diseases Due to the Bacillus mallei

Glanders Bacillus.—The *Bacillus mallei* (Loeffler and Schutz) is a slender rod, about as long as the tubercle bacillus, but thicker. It is non-motile. It stains irregularly with Loeffler's methylene blue, and is Gram-negative. It is easily grown on ordinary media like agar, blood serum,

and potato, but it is best isolated by means of animal inoculation (intraperitoneal injection of male guinea-pig, with recovery after two days from the testicle). Infection due to this bacillus is rare in man, and when met with, it has usually been contracted from the horse, an animal in which glanders is a contagious and fatal disease. Among human beings, it is stable-men, soldiers (cavalry), cab-drivers, and veterinarians that are most often infected.

(*a*) *Glanders and Farcy*

Definition.—An infectious disease, common in horses, rare in man, due to the *Bacillus mallei,* which gives rise to nodules (infectious granulomata) in the nose **(glanders)** and beneath the skin **(farcy).**

Man is most often infected by inoculation of the skin, occasionally, through the mucous membranes. Laboratory workers may be accidentally infected; among the pathogenic bacteria, the *B. mallei,* the *B. pestis,* the *B. anthracis,* and the *Micrococcus melitensis* are among the most dangerous to work with.

Symptoms.—The disease may be acute or chronic. It is believed that the incubation period is from 3 to 5 days.

In the **acute cases,** always fatal, the symptoms are those of septic infection starting from a cutaneous wound. After slight *prodromata* (headache, fever, malaise,) there is *local infiltration* and *ulceration,* with lymphangitis, and swelling of adjacent lymph glands. In less than a week, the signs of *general sepsis,* and of *metastases* appear. Painless swellings, quickly leading to suppuration and ulceration, appear in the skin (*farcy*). In addition, a red papular *eruption,* becoming pustular, appears between the 6th and the 12th day. A bloody discharge from the nose appears; abscesses develop in the muscles and in other organs; there is marked sweating; the patient loses strength; finally there is circulatory failure and death.

Occasionally, an acute nasal infection (*glanders*) is seen, causing nasal obstruction, with sanguineo-purulent discharge, dysphagia, hoarseness, and foul breath. Bronchitis and bronchopneumonia develop, and later general sepsis with metastases. The disease is accompanied by leukopenia.

In the **chronic form,** the onset is insidious, with pains in the limbs and joints, and slow development of local abscesses, followed by ulcers and cicatrization. This chronic form may last for years.

Diagnosis.—The anamnesis is helpful. In the acute cases, *typhus abdominalis, acute rheumatic fever* or *general sepsis* due to other bacteria may be simulated. The cutaneous lesions help to distinguish the disease from these, and the bacteriological examination, with guinea-pig inoculation, is decisive.

In the chronic cases, a **mallein test** (similar to the tuberculin test) may

be employed; a *complement-fixation test* has also been worked out (Schultz and Schubert), the antigen being made from the *Bacillus mallei*. An *agglutination test* has been much used in recognizing the disease in animals.

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18. Diseases Due to the Tubercle Bacillus

Tubercle Bacillus.—The *Bacillus tuberculosis* (Koch, 1882) occurs in four varieties, or races:

1. The human bacillus (*typus humanus*).
2. The bovine bacillus (*typus bovinus*).
3. The bacillus of *avian tuberculosis* (chicken, pheasant, pigeon, parrot).
4. The bacillus of cold-blooded animals (*turtle bacillus*, etc.). Morphologically, these races resemble one another closely. The 4th variety appears to be harmless for man.

Human beings are infected most commonly with the first, occasionally with the second, and very rarely with the third variety.

The tubercle bacillus is a long slender bacillus (Plate I, Fig. 1), often slightly curved and occasionally showing branching forms. In smear preparations, made from sputum containing tubercle bacilli, one sees usually groups of a few bacilli, lying parallel to one another, at an angle, or

across one another. The bacillus is non-motile, and does not form spores. It does not stain easily with the ordinary anilin dyes; it is Gram-positive and is *acid-fast* (like lepra bacilli, smegma bacilli and butter bacilli) owing to its content in wax.

The human type is not easily cultivated; it grows only at the body temperature, preferably on blood serum, glycerin agar, or bouillon or on Dorset's egg-medium; a dry scaly growth appears, taking several weeks to develop. For staining methods, see page 143. The tubercle bacillus occurs in the *sputum* in pulmonary tuberculosis, in the *feces* in intestinal tuberculosis, in the *urine* in urogenital tuberculosis, in the *pus* from carious bones and scrofulous glands, in the *skin* in lupus, and, sometimes, in the *blood* in general miliary tuberculosis.

Pathogenicity of the Tubercle Bacillus.—The guinea-pig is the most susceptible animal. Human beings are relatively insusceptible, even to the *typus humanus*. Though the majority of human beings are infected at some time or another, most people have sufficient resistance to prevent serious disease. For tuberculin tests, see page 172.

Cultures of the human type of the bacillus have but little virulence for cattle or for rabbits, producing no lesion, only a local lesion, or a mild and chronic disease; whereas cultures of the bovine type, inoculated into cattle or rabbits, cause a generalized, and rapidly fatal, tuberculosis.

Inoculation of a guinea-pig is a most important method for determining the presence or absence of tubercle bacilli, when they cannot be demonstrated by ordinary tests, or even by the antiformin method. If a guinea-pig be inoculated subcutaneously in the lower abdominal region, or, preferably, in the groin, the adjacent lymph glands can be extirpated at the end of 2 weeks and examined for tubercle bacilli in paraffin sections or in smears; moreover, if the injected material contains tubercle bacilli, the animal will die, and will show typical tuberculous lesions at autopsy.

Portals of Entry and Paths of Infection in Tuberculosis.—Human beings may be infected through the most different portals of entry, but the spread, in each case, from the infection atrium to other parts of the body occurs through the lymph paths (*lymphogenous tuberculosis*). A few bacilli may enter the blood and reach distant organs (*hematogenous infection*). In some cases, large numbers break through a vein into the blood and cause *general miliary tuberculosis.*

In considering the paths of infection in human tuberculosis, we try to determine: (1) how the tubercle bacillus entered the body to cause the oldest focal lesion, and (2) how, thence, the bacilli reached other organs, and caused the clinical symptoms.

An individual may be infected before birth (*congenital tuberculosis*, or *intra-uterine infection*); a majority, however, are infected after birth (*extra-uterine infection*), either from some other tuberculous human being

(directly or indirectly), or from tuberculous cattle. There is much dispute as to whether infection occurs most often through the digestive tract, or through the respiratory apparatus. In the former, the primary infection may involve the throat (tonsils) and the cervical lymph glands, or the intestinal mucous membrane and the mesenteric lymph glands, and thence spread through the lymphatics or through the blood to other parts of the body. In case of infection by the respiratory path, the bacilli are taken up by *inhalation*, infecting the mucous membrane of the bronchi and lungs, and extending to the bronchial lymph glands.

In human beings, tuberculous infections cause, as a rule, exquisitely *chronic* diseases, especially at first. In certain special conditions, *acute*, rapidly progressive forms appear (*galloping phthisis, miliary tuberculosis*). The tubercle bacillus may become disseminated in the body (1) by *contiguity*, (2) by the *lymph paths* (e. g., in polyserositis), (3) by *auto-inoculation* (e. g., infection of the larynx, or of the intestine, by tuberculous sputum from lungs), (4) by way of the *urine* (e. g., infection of the bladder from a tuberculous kidney), and (5) by way of the *blood* (hematogenous infection), as in chronic metastatic tuberculosis, and especially in acute general miliary tuberculosis.

Wherever the tubercle bacilli lodge in the body, there is a peculiar inflammatory reaction, with production of a nodule **(tubercle)**, gray at first, later becoming white, and, after central caseation, yellow. A *miliary tubercle* is about the size of a hemp seed, and histologically consists of one or more giant cells near the center, surrounded by a layer of epithelioid cells, or fibroblasts, outside of which is a layer of small mononuclear cells; the bacilli are often demonstrable in such nodules. Adjacent miliary tubercles often become confluent, to form later a single caseous mass (*conglomerate tubercles*). As a result of caseation, and of softening, tuberculous *cavities*, tuberculous *ulcers*, and tuberculous *fistulæ*, arise.

Any organ of the body may become tuberculous, though the thyroid gland and the muscles are rarely attacked. Tuberculosis shows a predilection, however, for certain organs (lungs, meninges, serous membranes, kidneys, urogenital system, bones). This *selective affinity* is sometimes a help in differentiating tuberculous from syphilitic lesions; thus, in bone, tuberculosis attacks most often the marrow (*caries*), especially that of the epiphyses, while syphilis frequently causes subperiosteal lesions and new formation of bone; in the male genitals, tuberculosis more often involves the epididymis, while syphilis is prone to attack the testicle itself.

(*a*) *Pulmonary Tuberculosis*

(*Pulmonary Phthisis, Tuberculosis pulmonum, Pulmonary Consumption*)

Only a brief epitome will be given here; for a fuller account see Part V, Diseases of the Respiratory Apparatus.

Three clinical groups of pulmonary tuberculosis may, for practical purposes, be considered (Osler):

1. Acute phthisis.
2. Chronic ulcerative phthisis.
3. Chronic fibroid phthisis.

i. Acute Phthisis

(Galloping Consumption, Phthisis florida)

A pneumonic form and a bronchopneumonic form are distinguishable. In the pneumonic form, we deal with *caseous pneumonia*, involving usually a whole lobe, or more. In the bronchopneumonic form, there is an acute caseous bronchopneumonia; it is especially common in children.

Symptoms.—The symptoms in the PNEUMONIC FORM are, at first, those of a frank lobar pneumonia, but no crisis occurs; the temperature continues elevated and the pulse accelerated. The sputum becomes mucopurulent and greenish in color (Traube). Signs of softening appear, and elastic tissue and tubercle bacilli become demonstrable in the sputum. Death may occur in a week, but some patients drag on for three months or more. Absence of breath sounds in the consolidated area is common, but there may be outspoken tubular breathing. The fever is more remittent than in lobar pneumonia.

In the BRONCHOPNEUMONIC FORM, there is high fever, tachycardia, tachypnea, with chills and sweating. Signs of bronchopneumonia gradually become demonstrable in the lungs. The disease is, in children, often preceded by measles, or by whooping-cough.

ii. Chronic Ulcerative Phthisis

This is the commonest form of pulmonary tuberculosis. It occurs most frequently in individuals with the so-called *habitus phthisicus* (pallor, emaciation, poor muscular development, small bones, paralytic type of thorax). On examining these patients, one often sees the brown discoloration of pityriasis versicolor on the chest.

Anamnesis.—The patient usually gives a family history of tuberculosis (parents, sibs, conjugal partner, children), stating that one or more members have suffered from consumption, pleurisy, scrofula, or meningitis. The patient himself may have earlier suffered from enlarged cervical glands, corneal lesions, or bone troubles (scrofula), or he may give a history of cough, of hemoptysis, of hoarseness, or of one or two attacks of pleurisy earlier in life. On questioning the patient, his general circumstances and mode of living should be gone into; his occupation (dust, exposure) and habits (alcoholism, work, sleep) should be asked about. Recent loss of weight is an important symptom, and, in following a case,

he keeping of a body-weight chart may be more important than a t
ure chart.

Physical Findings in the Lungs.—In the first stage (PHTHISIS
ENS) one finds signs of apical bronchitis (moist or dry râles, es
fter coughing), with enfeebled, roughened, or cogwheel-like, res

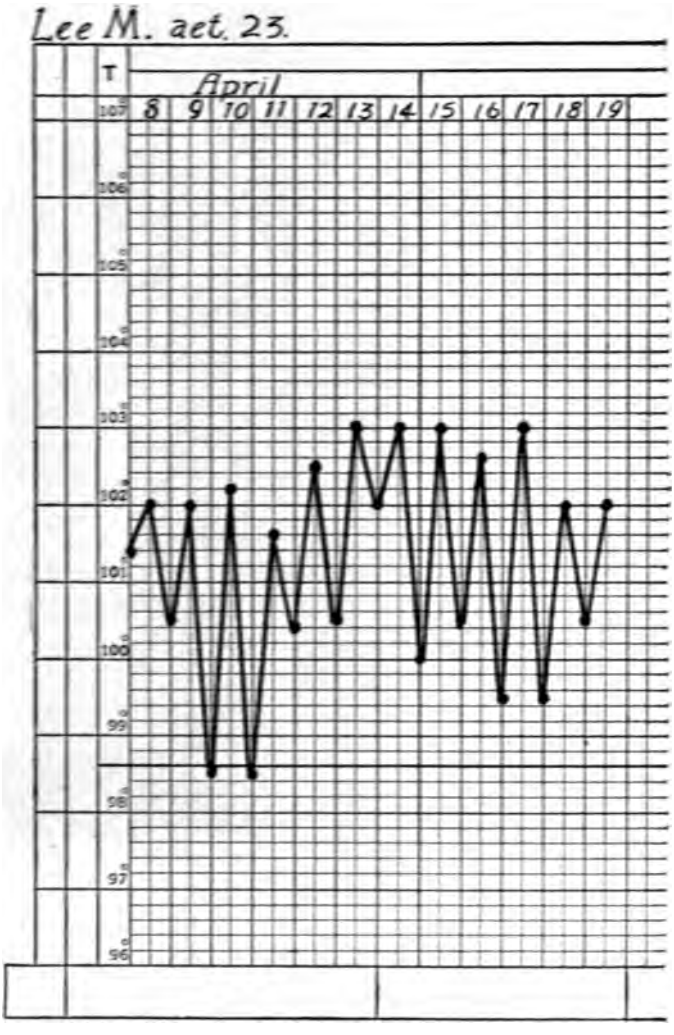

Fig. 81.—Pulmonary Tuberculosis. (Personal Observation.)

murmur. Expiration is often prolonged. There may or may not
dullness on percussion. A slight delay in expansion of the affec
can often be made out. In such patients there is usually a litt
ing cough, with scanty sputum, and this may contain tubercle

("open case"), or they may yet be absent ("closed case"). A hemoptysis may have been the first symptom noticed.

In the second stage (PHTHISIS CONFIRMATA) the physical signs of infiltration can be made out in the upper part of one upper lobe; there is dullness in front and behind with bronchial breathing, consonating crackles, and lessened expansion. The sputum is more abundant, is mucopurulent, and contains tubercle bacilli. The röntgenogram taken after a deep inspiration, the patient holding his breath, shows infiltration in areas corresponding to the dullness on percussion, and often beginning infiltration in the other lung.

Instantaneous röntgenography with use of an intensifying screen gives the best negatives, as regards details; in women the breasts should be pressed lateralward as far as possible by the plate holder. It is well to make special small plates of the apices with the aid of a diaphragm; the anticathode should be placed close to the first intercostal space, for otherwise this space is likely to be hidden by the second rib; the normal radiation should be adjusted for the jugulum, the head being bent well back. Good röntgenograms of the upper aperture of the thorax can be taken by the method of Hart and Harras (1908). Stereoscopic plates are very valuable for exact diagnosis. (See Part V.)

In the third stage (PHTHISIS CONSUMMATA) there are signs of widespread infiltration in both lungs, and of cavity formation. The cavities are recognizable on physical examination by the loud bronchial, or amphoric sounds audible over them, with tympany and changes of pitch in different positions (Wintrich, Friedreich, Gerhardt). (See examination of the lungs.) The sputum is often nummular and crowded with tubercle bacilli, often in large masses from the walls of cavities; it may contain elastic fibers also.

In most cases there is *fever,* often of HECTIC type, especially in the third stage. The patients suffer from night sweats, and, sooner or later, become emaciated. Digestive disturbances are troublesome; it is often of these that the patient complains when he first consults his physician. Not a few of the cases present signs of Graves's disease (tachycardia, tremor, palpitation, nervous symptoms).

iii. Chronic Fibroid Phthisis

This is a very common form of pulmonary tuberculosis, the duration of which may be 10 to 20 years, or more. The patients are usually afebrile, much of the time, but they suffer from paroxysmal cough, and from dyspnea on exertion. The sputum is purulent, and contains tubercle bacilli. Complicating bronchiectasis is common, with fetid bronchitis.

The physical signs of *shrinking of the lung* (retraction of the affected side); dislocation of adjacent organs; vicarious emphysema of unaffected lung, enlargement of the right heart and hippocratic fingers are demon-

strable. The cases are sometimes confused with pulmonary cirrhosis, due to anthracosis, etc.

Complications of Pulmonary Tuberculosis

The more important are (1) hemoptysis, (2) tuberculous pleuritis, (3) mixed infections (pyogenic cocci, influenza bacilli), (4) laryngeal tuberculosis, (5) intestinal tuberculosis (swallowing of sputum), (6) pneumothorax, and (7) amyloid disease.

(*b*) *Lymphadenoid Tuberculosis*

(*Tuberculosis of the Lymph Glands, Scrofula*)

This may occur at any age, but is most common in children, affecting most often the bronchial, though, also often, the cervical, the mediastinal, or the mesenteric glands (*tabes mesenterica*), or, occasionally, all the lymph glands of the body simultaneously (*generalized tuberculous lymphadenitis*).

Scrofulous children are usually pale and delicate, and are very subject to chronic catarrhal inflammations. Thus they often have nasal catarrh, with thickening of the nose and of the upper lip. They are often victims of ozena, of hypertrophied tonsils, of suppurative otitis media, of phlyctenular conjunctivitis, and of recurring blepharitis. Many of them suffer from chronic skin eruptions (*eczema, prurigo, lupus, lichen scrofulosorum,* etc.). In addition to the enlargement of the lymph glands, they frequently suffer from tuberculous diseases of the bones and joints (*hip-joint disease, white swelling of the knee, caries of the spine*), and from that form of chronic osteomyelitis of the phalanges of the fingers and toes, with spindle-shaped expansion of the compact substance known as *spina ventosa.* (See also *Lymph Glands,* under Diseases of the Blood and of the Blood-Building Organs.)

Diagnosis and Differential Diagnosis.—This is usually easy, but enlarged lymph glands, especially in the neck, may be due to causes other than tuberculosis, for example, long standing *pediculosis* causing eczema of the head, swelling of the cervical lymph glands, blepharitis and coryza. *Hereditary syphilis* should be ruled out (Hutchinsonian teeth, keratitis syphilitica, Wassermann reaction, etc.). In tuberculosis of the bronchial glands, the cough may resemble that of *whooping-cough,* though the stridor is more often expiratory than inspiratory. The percussion sounds and the x-ray findings are characteristic.

In tabes mesenterica with enlarged and tympanitic abdomen and with diarrhea, marked emaciation and anemia, the diagnosis can usually be easily made.

In generalized tuberculous lymphadenitis, the affection may be mistaken for *Hodgkin's disease.* Cultures from, and histological examination of, an excised gland, and the differential count of the leukocytes will decide.

(c) *Tuberculosis of the Serous Membranes*

(Tuberculous Serositis)

Acute or chronic tuberculosis of any one of the serous membranes may occur (pleuritis, pericarditis, peritonitis), or two or more cavities may be simultaneously involved (polyserositis, polyorrhomenitis).

The diagnosis depends upon the family history, the physical signs, the presence or absence of signs of tuberculosis elsewhere in the body, the examination of the exudate (cytodiagnosis, tubercle bacilli, animal inoculation, q. v.), röntgenoscopy and röntgenography, and tuberculin tests.

These diseases are described more fully under Pleuritis and Peritonitis.

(d) *Tuberculosis of the Joints*

(Arthritis tuberculosa)

This was formerly known, especially in the knee, as "white swelling" (*tumor albus*). The joints most frequently affected are the hip and the knee, though the elbow, wrist, shoulder, or ankle may be involved. (See also Part XI.)

Tuberculosis of the Hip-Joint

(Coxitis tuberculosa)

A child complains of tiring easily, begins to limp on walking and to complain of the leg hurting. On examination, the gluteal fold on the affected side may be obliterated, and the musculature on that side somewhat atrophic. Sometimes the child complains more of the knee than of the hip, but physical examination shows that the knee joint is normal. If the child be undressed and laid upon a flat table, with both legs outstretched, there is found to be lordosis of the lumbar spine, so that the hand can be thrust underneath. If, next, the back be laid flat upon the table, the knee on the affected side will be somewhat lifted, owing to slight flexion of the hip. Sometimes, along with this, there is abduction and lateral rotation, sometimes adduction and medial rotation.

The movements of flexion, extension, adduction, abduction, and rotation of the affected joint are limited. The child tries to use the lumbar spine instead of the hip, keeping the hip rigid. He thus moves his pelvis without his thigh. Such rigidity of the hip may be due either to muscle spasm or to changes inside the joint itself (ankylosis). The earliest movements to be limited are, as a rule, abduction and rotation. If one try to abduct the lower extremity rather quickly, and this cause adductor spasm, it is strong evidence of coxitis, even though movements in other directions are normal.

In some instances, a cold abscess beneath the anterior superior iliac

spine is palpable. The inguinal lymph glands may be enlarged. There is often tenderness on pressure on the anterior surface of the joint, just below the middle of Poupart's ligament. If the knee be held stiff, a sudden blow on the heel, shoving the femur upwards, or a blow over the trochanter, may cause pain in the hip-joint.

Differential Diagnosis.—1. From a *non-tuberculous arthritis*—more acute onset, in the acute cases; in the chronic cases, the older the patient, the less probable tuberculosis; x-ray examinations are often decisive.

2. In the painful stage, from *coxa vara*—limping due to shortening, not to pain; foot strongly rotated lateralward; high position of trochanter; röntgenogram.

3. From *congenital luxation of hip*—shortening of spinomalleolar distance; abnormal mobility of thigh; high position of trochanter; head of femur palpable near trochanter; lumbar lordosis; röntgenogram.

4. From *diseases independent of the hip-joint*—old abscess from spondylitis; perinephritic abscess; appendiceal abscess; hydrops of iliac bursa; sciatica; hysteria.

In any of these, there may be a flexion-contracture of the hip, or pains in the region of the hip, with painful limping.

ii. Tuberculosis of the Knee-Joint

(*White Swelling, Tumor albus, Gonitis tuberculosa*)

(a) **Simple Effusion.**—This is most common in children, in whom it is the commonest form of serous gonitis. From the beginning the capsule is thickened at the upper recess of the joint and over the two condyles of the femur, and the joint always feels hot, even when the disease has lasted for months. Movements of the joint may be only slightly, if at all, limited, and muscular atrophy comes late.

Differential Diagnosis.—In the differential diagnosis, we must distinguish it: (1) from *chronic infectious arthritis* (periarticular); (2) from *congenital lues* (choroiditis, teeth, Wassermann); (3) from *hemophilic joint* (blood on aspiration, typical röntgenogram, family of bleeders).

(b) **Fungous Gonitis.**—In this form, the capsule is diffusely thickened. In the differential diagnosis we must consider (1) *luetic arthritis,* (2) *sarcoma,* and (3) *lipoma arborescens.*

(e) *Tuberculosis of the Bones* (*Caries*)

The process begins in the bone-marrow. The bones most frequently affected are (1) those of the *spine,* (2) the bones of the *pelvis;* but *other bones* (os calcis, humerus, jaw, femur, ribs, skull, sternum, tibia) may be affected.

i. Spondylitis tuberculosa (Caries of the Spine)

In caries of the spine, or **Pott's disease of the spine** (*spondylitis tuberculosa*), the diagnosis is easy when the vertebra has softened enough to give rise to a projecting angle or **gibbus.** One has, then, only to look at the back to make a diagnosis, as the angular bend of the spondylitic kyphosis is very characteristic. If a projecting portion of the spine involve more than one spinous process, we think of rachitic deformity rather than of tuberculosis. Ordinary scoliosis and kyphoscoliosis are easily distinguishable.

Fig. 82.—Caries of Spine. (Pott's Disease.) Note the Gibbus in the Thoracic Spine. (Med. Service, J. H. H.)

In adults, there may be no gibbus and no cold abscess. Sometimes the diagnosis can be made in a child before a gibbus or a cold abscess has appeared (stiffness of the spine, crying when lifted from the bed, x-ray examination, tuberculin test).

In adults, *pain* referred to the umbilical region, to the back of the neck, or along the sciatic nerve, or a pain in the back on descending stairs, or on hitting the boot against a stone in the street, should make one think of spondylitis. In beginning spondylitis of the cervical spine, a sudden movement of the head may cause pain in the lower extremities.

On examining the *movements* of the spine, the patient should always be wholly undressed. Flexion, extension, and the lateral movements of the spine should be tested.

Pressure in the long axis may cause pain. Pressure with the thumb upon the individual spines of the vertebrae may elicit a tender spot, though this is not usually found.

The application of a *hot sponge* over the individual spines may cause pain in the affected area.

In looking for *cold abscess,* which sooner or later appears in 25 per cent to 50 per cent of the cases, and may be the first tangible symptom, we examine the following localities: (1) posterior pharyngeal wall, (2) the

side of the neck, (3) axilla and infraclavicular fossa, (4) the back, (5) between the last rib and the crest of the ilium in the lumbar region, (6) above and below Poupart's ligament (psoas abscess), (7) beneath the muscles of the buttock, (8) in the iliac fossa (iliac abscess), (9) in the perineum, and (10) in the mediastinum.

Differential Diagnosis of Cold Abscess.—Such cold abscesses must be differentiated: *in the cervical region,* from (1) lipomata, (2) bronchial cysts, (3) esophageal diverticula, and (4) strumata; *in the lumbar region,* from (1) lipomata, (2) lumbar hernia, and (3) perinephritic abscess; *in the iliac fossa,* from (1) ileocecal tumors, (2) appendiceal abscess, (3) abscess from osteomyelitis, and (4) parametritis; *in the inguinal region,* from (1) hernias, (2) hydrocele of the spermatic cord, and (3) hygroma of the subiliac bursa; *in the perineum,* from (1) dermoid cysts, and (2) periproctitic abscess.

The origin of a cold abscess with *fistula* formation can often be traced by Beck's method (röntgenogram after injection with vaselin containing 20 per cent bismuth carbonate, or 30 per cent zirconium oxide [Caution!]).

The *differential diagnosis from non-tuberculous spondylitis* is usually easy by means of the constitutional symptoms, the x-ray, and immunological tests.

(*f*) *Tuberculosis of the Skin*

Clinically, this may assume any one of several different forms, the etiological unity of which is shown by the demonstration of the tubercle bacilli in the lesions by microscopical examination, culture or animal experiment, by the histological structure, and by focal reactions on injection of old tuberculin. Whether or not there are also skin lesions due only to the toxins of bacilli (so-called tuberculides) is still disputed. The forms of skin disease absolutely established as local lesions due to the tubercle bacilli are (1) lupus vulgaris, (2) scrofuloderma, and (3) ulcerative acute miliary tuberculosis of the skin (tuberculosis cutis propria). It seems probable that (4) lichen scrofulosorum (tuberculosis maculo-papulosa aggregata) belongs here also.

Tuberculosis of the skin may be primary or secondary to tuberculosis of internal organs.

i. Lupus vulgaris

Definition.—A chronic form of tuberculosis of the skin, characterized by a peculiar primary efflorescence known as the lupus nodule.

Symptoms.—A *lupus nodule* is a conglomerate of miliary tubercles, appearing as a sharply circumscribed, transparent, yellowish or brownish-red macule, varying in size from the head of a pin to a pea, which does not disappear when pressed upon by a glass slide but becomes even more distinct. Such spots may be the only sign at the beginning (*lupus*

maculosus); later, the epidermis on the surface may desquamate (*lupus exfoliativus*). Later still, there may be irregular central scarring (*lupus serpiginosus*). Sometimes the infiltration rises above the level of the skin, and flat brownish-red thickenings appear (*lupus tuberosus*). If there be marked proliferation of the connective tissue beneath, tumor-like nodules arise (*lupus hypertrophicus*). Lupus most often attacks the face (nose, cheeks, upper lip). If the neck, trunk, and extremities are affected, a serpiginous lupus is usually seen. In the hand, whole phalanges may be lost in the older cases (*lupus mutilans*), as in leprosy. Occasionally, the mucous membranes are attacked.

The disease begins usually in childhood, is extremely chronic, and shows periods of improvement followed by exacerbation.

ii. Scrofuloderma

Definition.—A tuberculosis of the skin, beginning in the subcutaneous layers, or in the deeper layer of the cutis.

Symptoms.—Two forms are met with, one giving the impression of a direct infection of the skin from without or through the blood, the other secondary (by extension) from tuberculosis of bones, lymph vessels and glands. It is a disease of youth. The course is chronic and painless.

Differential Diagnosis.—It is distinguished (1) from acute inflammatory processes (*furuncles*) by its chronicity and its painlessness; (2) from *gumma* (therapeutic test, Wassermann reaction, negative local reaction to old tuberculin, no tubercle bacilli in tissues on histological examination).

iii. Ulcerative Miliary Tuberculosis of the Skin

This is a rare condition, seen in connection with advanced tuberculosis of the internal organs; it appears usually around one of the orifices (mouth, nose, anus) as shallow, granulating, painful ulcers, in which, often, miliary tubercles are visible. It may be mistaken for soft chancre, or for syphilitic ulcer. The disease appears to be due to auto-inoculation from the neighboring orifice.

iv. Lichen scrofulosum

This also is a rare disease met with in children who suffer from tuberculosis of the lymph glands, bones, or cornea. The disease presents itself in the form of minute nodules, the size of a hemp-seed, arranged in groups, or in circles. They are of a pale yellow, or brownish-red, color, and early show superficial desquamation. The trunk is most often affected (sacral region, lateral wall of thorax); occasionally, the face or the extremities may be involved.

The course is chronic. Tubercle bacilli have been demonstrated in the lesions microscopically and by animal inoculation. There are no subjective symptoms.

The disease must not be confused (1) with *lichen pilaris* (no grouping, extensor surfaces), (2) with *lichen ruber,* or (3) with *lichen syphiliticus* (Wassermann test).

(*g*) *Tuberculosis of the Urogenital System*

Any one of the urogenital organs in the male or female may be affected. After one organ is infected, others frequently become involved by extension, and in late stages it may be difficult to determine the primary site.

Acid-fast bacilli in the urinary sediment (when urine has been drawn by catheter to avoid the smegma bacillus) give positive evidence of infection. If infection be suspected and the bacilli are not discoverable microscopically, inoculation of guinea-pigs should be resorted to.

Chronic Renal Tuberculosis (Phthisis renum).—The infection is of hematogenous origin in 90 per cent of the cases (George Walker). Clinically the signs are those of pyelonephritis. The urine contains albumin and pus, sometimes blood and tissue shreds, elastic fibers, and tubercle bacilli, and there usually is fever and emaciation. In urethral tuberculosis, the thickened urethra can sometimes be felt through the rectum, or in women through the vagina. Catheterization of the ureters should be done, to see whether both sides are affected, or only one. In renal tuberculosis, bladder tenesmus may be most troublesome, and frequency of urination is an early and constant symptom. Dull aching pain in the lumbar region is frequently complained of and a tender enlarged kidney may be palpable. Hematuria frequently occurs, and x-ray examinations may show irregular enlargement of the kidney. (See also Part X.)

Tuberculosis of the *bladder, prostate, seminal vesicles* and *testes* is comparatively rare, though tuberculous *epididymitis* is fairly common.

Tuberculosis of the Fallopian Tubes (Salpingitis tuberculosa).—This is a common disease in women, usually bilateral. The masses are easily felt on bimanual palpation, especially under an anesthetic. The differential diagnosis must be made from *gonorrheal salpingitis* and from *tubal pregnancy.*

Tuberculosis of the ovary and uterus are rare.

Tuberculosis of the placenta in pregnant women is not uncommon when pulmonary tuberculosis exists.

Tuberculosis of the mammary gland sometimes occurs at the menopause and later, in women. There is irregular induration, sometimes retraction of the nipple, and frequently ulcers and fistulae, following cold abscess. The course is chronic. The axillary glands are enlarged.

(*h*) *Tuberculosis of the Meninges* (*Meningitis tuberculosa*)

This disease occurs most often in children (2-5 years), but is not infrequent in young adults.

Symptoms.—The onset is insidious, often following a period of poor health, or an attack of measles, or whooping-cough. The child emaciates, looks badly, seems apathetic, suffers from constipation, and is restless in its sleep. Later the temperature begins to rise, and there is vomiting. The pulse is slow and irregular (though often very rapid at onset). After complaining of pain in the head for a variable period, the child becomes dull, sleepy, delirious, often gritting its teeth in its sleep. The neck becomes rigid, there is often general hypertonicity of the muscles; and there is gen-

Fig. 83.—Tuberculous Meningitis. Universal Tonic Spasm; Automatic Movements of the Left Half of the Body; Scaphoid Abdomen; Extreme Emaciation. (After J. Ibrahim, in E. Feer's "Lehrb. d. Kinderheilkunde," published by G. Fischer, Jena.)

eral cutaneous hyperesthesia (*period of irritation*). The pupils may be unequal and sluggish in reaction; choked disk is common. Boat-shaped retraction of the abdomen is an important sign.

In the *paralytic stage,* the child becomes comatose, the pupils are dilated; facial paralysis, eye muscle paralysis, or hemiplegia may develop. The pulse becomes rapid; Cheyne-Stokes breathing may appear. Leukocytosis is not uncommon. Death in convulsions commonly occurs in the third week. In the more chronic cases of the disease, convulsions may or may not be present. (For a further description, see Diagnosis of Diseases of the Nervous System.)

Diagnosis.—Tuberculous (bacillary) meningitis should always be thought of when a child predisposed to tuberculosis (heredity, scrofula, preceding attack of whooping-cough, or measles) becomes apathetic, vomits without apparent cause, and develops a slow, irregular pulse. Whenever the disease is suspected, lumbar puncture should be done. A turbid fluid under heightened pressure, with increased lymphocytes rather than polymorphonuclear leukocytes, speaks for tuberculous meningitis. (See Exami-

nation of Cerebrospinal Fluid.) On careful search, tubercle bacilli can usually be demonstrated in the fluid, either by staining a smear of the fibrin-film that frequently forms on standing, or by animal inoculation (J. Hemenway). Sometimes the cerebrospinal fluid is clear in tuberculous meningitis, and still tubercle bacilli may be demonstrable in it.

Differential Diagnosis.—(1) From *epidemic cerebrospinal meningitis*—polymorphonuclear cells and meningococci in spinal fluid; sudden onset; (2) from *typhoid fever with meningismus*—blood culture; lumbar puncture; (3) from *uremia*—urinary examination; phenolsulphonephthalein test; lumbar puncture.

(*i*) *Acute General Miliary Tuberculosis*

Definition.—A disease due to the sudden overwhelming of the blood with tubercle bacilli, with formation of innumerable miliary tubercles in the organs. The bacilli enter the blood through an eroded vein, or through the thoracic duct (caseous lymph gland; caseous pulmonary tuberculosis). More rarely, miliary tuberculosis follows tuberculosis of the intestine and mesenteric lymph glands, of the medulla of the adrenal, or of the genito-urinary system.

Symptoms.—These are partly due to the multiple tubercles in the organs, partly to the toxins of the tubercle bacilli.

Three principal types are distinguished: (1) the typhoid form; (2) the meningeal form, and (3) the pulmonary form.

(1) *The Typhoid Form.*—Here the toxic effect dominates the clinical picture. The onset is often acute, with chill, vomiting, and high fever, which may be continuous or slightly remittent. In addition, one sees tachycardia, tachypnea, cyanosis or pallor, delirium, often splenic tumor, meteorism, and diarrhea; occasionally rose spots and sometimes herpes. Death usually occurs in the third week, in coma. The absence of the *B. typhosus* in the blood culture, the small rapid pulse, the cyanosis, and the tachypnea distinguish it from typhoid. Sometimes a focus of tuberculosis is demonstrable in the body, and occasionally the bacilli are demonstrable in the blood by the method of Jessen and Rabinowicz.

These authors draw 5-10 c.c. of blood into an equal amount of 2.5 per cent citric acid. The mixture is carefully shaken, avoiding foam formation, allowed to stand in the ice-box for several hours, and then thoroughly centrifugalized. Smears are made from the sediment and stained for tubercle bacilli.

I have often looked for tubercles in the choroid, a much vaunted pathognomonic sign, but in my experience it is not easy to find them.

(2) *Meningeal Form.*—Here the symptoms are largely due to the metastatic infection of the meninges and of the brain. The signs are those of tuberculous meningitis (q. v.).

(3) *Pulmonary Form.*—If the symptoms of toxin effect, or of meningeal infection, be not marked, the patient's appearance may call attention rather to the pulmonary disturbances. The principal symptoms then are fever, cough, pain in the chest, tachycardia and tachypnea, cyanosis, signs of a diffuse general bronchitis in the lungs, or a wide-spread bronchopneumonia; occasionally, there is blood-tinged sputum. Death occurs in from 3 to 5 weeks, the approach to death resembling that in acute bronchopneumonia.

Differential Diagnosis of Miliary Tuberculosis.—Besides excluding (1) *typhoid fever,* (2) *epidemic cerebrospinal meningitis,* (3) *bronchopneumonia,* and (4) *pneumonia of pyogenic origin,* the following diseases should be ruled out: (5) *septicemia,* especially in the puerperal period (blood culture, leukocytosis); and (6) *malaria* (parasites; temperature curve; therapy).

Occasionally miliary tuberculosis is combined with typhoid fever, or with sepsis, in which event the elect may be deceived.

The tuberculin reactions are rarely of any assistance in the diagnosis of these acute types of tuberculosis. (See Tuberculin Reactions.)

Some of the Factors Influencing the Course of Tuberculosis

We shall now discuss some of the factors influencing the course of tuberculosis, referring briefly to the relations of tuberculosis (1) to pregnancy, (2) to marriage, and (3) to the use of alcohol.

Tuberculosis and Pregnancy.—The unfavorable influence of pregnancy upon the course of tuberculosis has long been recognized, though now and then one hears a report of a favorable influence being exerted. Thanks to the studies of Rosthorn and Fraenkel, we have data concerning this point derived from exact observation of a large number of cases. These authors assert that, in apical processes that are not very extensive, or in cirrhotic processes in the lungs, whether accompanied by fever and emaciation or not, provided other complications are absent, there is no indication for the interruption of pregnancy. In such cases, a waiting attitude should be assumed, the tuberculous process in the lung being closely watched and the patient, of course, being given every hygienic and dietetic advantage. In case, despite careful treatment, there should be no improvement in the condition, no increase in the body weight or diminution of the fever, the question of interruption of the pregnancy, even in apparently mild cases, may be considered.

In patients in whom the tuberculous process is progressive, and especially when it is florid, with signs of high fever, rapid emaciation, and complications, especially if there be tuberculosis of the larynx, the interruption of pregnancy is distinctly indicated.

Artificial abortion, if it is to be done, should be carried out as early as possible, after which it may sometimes be possible to arrest the tuberculous process.

Every tuberculous woman who becomes pregnant should be kept under the strictest medical supervision, for if pregnancy is to be interrupted it should be done early in its course. Interruption of an advanced pregnancy is a serious matter and may be even as dangerous for the tuberculous woman as to allow the pregnancy to proceed to its natural termination.

Laryngologists and obstetricians have frequently emphasized the important relations existing between pregnancy and laryngeal phthisis; the majority agree that tuberculosis of the larynx is a definite indication for artificial abortion (Kuttner), though Rosthorn suggests that no general rule be set up, each case being rather considered and solved for itself. There can be no doubt that laryngeal tuberculosis, even in its early stages, is a highly dangerous complication in pregnancy, since even a mild, and otherwise relatively benign, tuberculous process in the larynx may, under the influence of pregnancy, assume a malignant and progressive character (Glas and Kraus). The symptoms rapidly increase, owing to the increased burden thrown upon the body as a whole, and to the interference with respiration, due to the high position of the diaphragm. The air exchange in the lungs and the expectoration are interfered with; everything that favors the extension of a pulmonary tuberculosis also exercises a deleterious influence upon the laryngeal tuberculosis.

Any pregnant woman who complains of hoarseness, or of difficulty in swallowing, should be examined by a laryngological specialist, and be kept under close observation, in order that any exacerbation of the local process may be recognized as soon as possible.

Tuberculosis and Marriage.—Conjugal tuberculosis is, as is well known, quite common; it is stated, variably, to exist in from 3.4 per cent to 39 per cent of the cases, the different statistics depending probably upon the difference in social classes studied. Of the two partners, it is the healthy wife who is the more endangered, since she, in caring for a sick husband, is more closely tied to the house than the husband who, having a sick wife, continues his work outside and leaves the care of her to others.

Both pulmonary and urogenital tuberculosis are common in conjugal tuberculosis, the urogenital tuberculosis being usually secondary to a primary pulmonary or to peritoneal tuberculosis, though it may sometimes be primary (q. v.).

The family practitioner has often to decide the question of marriage for a tuberculous person. No absolute rule dare be laid down; each single case must be considered for itself, and the decision entails a heavy responsibility. Persons suffering from fresh, progressive, tuberculous changes certainly should not marry, no matter how slight the process is; only after the condition has become stationary and the general state favorable, and after a period of at least three years has elapsed since the beginning of the disease, dare we, except in very unusual instances, consent to a marriage. Several other factors have to be borne in mind: First, whether it is a love-match, or a *mariage de convenance;* if the former be forbidden, the depressing mental effect will be greater than in the latter instance, while permission to marry when a suitable condition has been reached may be a strong spur to the patient to do everything possible for recovery. Again, the age of the patient should be considered; the younger the patient, the more prone is the tuberculous process to revival; moreover, excesses coincident to marriage and the bearing of children are less likely to occur in older persons than in the young.

Certainly no marriage should be contracted by a tuberculous person unless the healthy prospective partner has been previously fully informed regarding the infection in the other, and its dangers as well as the necessary modifications of life have been discussed.

Pecuniary circumstances have also to be considered. Among people of means who can command the best hygienic and dietetic conditions and who will not be compelled to engage in the struggle for existence, marriage may be permitted, when in opposite conditions it might be highly dangerous.

The question as to whether the marriage of two persons who are both tuber-

culous may be permitted, sometimes comes up. Obviously, should such a marriage take place, an agreement to a childless marriage should be arrived at beforehand. From a eugenic standpoint, it would seem wrong to burden offspring with a double tuberculous heredity.

Alcoholism and Tuberculosis.—The question as to whether alcohol plays any rôle in the origin of tuberculosis has been much discussed. Statistical studies indicate that it plays no important part; thus females are seldom the subject of alcoholism, according to statistics 16 times less than men, but tuberculosis is half as common in women as in men; moreover, many human beings sicken of tuberculosis at a period in life in which alcoholism plays no part (lymph gland tuberculosis in children). In as far as alcoholism leads to poverty, and to bad hygienic, dietetic and social conditions, it can of course contribute to the causation of tuberculosis.

The question as to whether the tuberculous patient shall, or shall not, use alcohol as a therapeutic agent, as a food, or as a luxury, has also been much discussed. Here again, the answer must be an individual, not a general one. Moderate amounts of alcohol seem to be no more harmful to tuberculous persons than to healthy people. Highly nervous people, or those who have a tendency to hemoptysis, should, of course, avoid alcohol. As a remedial agent, alcohol sometimes finds a place in tuberculosis as a stimulant, just as in other infectious diseases. It is also used by many physicians for patients who suffer from night sweats, or who have much fever. Finally, the pleasurable effects of a glass of wine, or of other substances containing alcohol, in moderation, may be argued as an advantage; especially in patients with a tendency to emaciation, the property of alcohol as a protein-sparer and fat-sparer is emphasized by many authorities. Sometimes, a patient who suffers from anorexia may eat better if a little wine, or beer, be given with his food. Certainly, all excess is to be avoided. There are many physicians who believe that alcohol should be strictly prohibited in tuberculosis and in all other diseases; it is not my purpose, however, to enter here upon a discussion of the advisability of total abstinence.

i. General Remarks on the Early Diagnosis of Pulmonary Tuberculosis in Adults

The general practitioner must depend, in the first place, upon the time-honored methods of examination, though in doubtful cases he may call upon accessory aids. The *anamnesis* is of very great importance, special attention being paid to the family history, the history of previous disease, the social and hygienic conditions under which the patient has lived, and the opportunities for contact-infection.

On *inspection,* the general "size-up" of the patient is important, though, in making an early diagnosis, it must be remembered that persons in apparently blooming health and of robust constitution may have the disease. It is, of course, much more common in people with the habitus phthisicus (see above). The thorax should be examined for stenosis of the superior aperture (W. A. Freund), due to calcification of the first costal cartilage. Delayed expansion at one apex on inspiration or a retraction as the result of a pleuritic exudate will also be manifest on inspection.

On *palpation,* the state of tension of the tissues in the supraclavicular and supraspinous fossæ on both sides should be tested, since, as Dünges has

pointed out, a diminished tonus points to a beginning retraction on that side.

The more important findings are to be made out on *percussion* and on *auscultation,* especially the latter. We cannot expect changes in the percussion note before the lesion has reached a certain grade. The infiltration must involve an area measuring 4-6 cm. by 2 cm. to cause dullness on percussion. I am inclined not to lay much weight on *very slight* differences in the percussion note at the two apices, since those who have most experience in the early diagnosis of tuberculosis may be in error regarding the significance of a slight apical dullness (L. Hamman). Still, careful percussion of the apices should be undertaken, and we pay attention not only to the sound produced, but also to the resistance felt by the pleximeter finger. It is well to compare also the note on percussion on both sides at the end of inspiration and at the end of expiration. The *first percussion signs* of infiltration are (1) a shortening of the percussion sound, and (2) an enfeeblement of the normal lung resonance. Only later, when the infiltration has become more marked, or the pleura thickened, can we expect to find dullness or flatness.

It has long been known that the right apex may occupy a little lower position than the left, even in entirely healthy people, and that, in patients with chronic nasal obstruction, there may be a non-tuberculous collapse-induration of the right apex (Baumann). Aside from this, a depression of the upper limit of lung resonance points to infiltration or retraction. Normally, the lung resonance should extend for from 3-5 cm. above the clavicle, and behind to the level of the 7th cervical spine.

The exact determination of the lower lung limits is also important, since, in most cases of incipient phthisis, the diaphragm on the affected side moves sluggishly or not at all during respiration, owing to diffuse adhesions of the costal pleura with the diaphragmatic pleura. Röntgenoscopy is a help here.

On *auscultation,* change in the breath sounds, especially a roughening or a weakening of inspiration, or a prolonged and roughened expiration at one apex, is very suggestive of a tuberculous process, especially if these findings be confirmed on repeated comparative auscultation of both apices.

The presence of râles at one opex, especially after coughing, is a most important auscultatory sign. Such râles may be present even when the breath sounds are as yet unaltered. Their presence, on repeated examinations, is pathognomonic for "apex catarrh."

At first, these râles consist of a few fine crackles, or crepitations. Later, coarser râles may be heard, and when infiltration has begun, they become consonating. As soon as the infiltration has reached a certain grade, the breathing loses its vesicular character and becomes bronchial. In older persons, a pulmonary tuberculosis may be masked by an asthma or

by an emphysema and then the diagnosis is hard to make, on account of the rarity of the association of tuberculosis with these conditions.

The *vocal resonance* is increased over infiltrated areas and especially over cavities, but enfeebled behind pleuritic exudates. Increased vocal resonance may appear at a period before auscultation of the breath sounds or percussion can demonstrate an infiltration. Later on, as the process advances, the voice sounds may diminish in intensity.

A *circumscribed pleurisy* with friction rub may be the first sign of early tuberculosis, especially in the upper lateral regions of the thorax.

It is unusual to find beginning tuberculosis associated with arterial hypertension. Usually, the *blood pressure is lower than normal* in tuberculous patients.

Among the conditions suggestive of a nearly latent, or larvate, form of tuberculosis may be mentioned: (1) a *chlorotic blood state* with the symptoms of chlorosis, (2) unexplained *digestive disturbances* (anorexia, acid eructations, meteorism, hyperacidity, atony), (3) *neurasthenic states*, (4) unexplained *pleurisy*, especially of insidious type, with recurrences, (5) *loss of weight*, and (6) *low fever*. In the so-called active-latent form of early tuberculosis the cardinal symptoms are fever, emaciation and sweats.

In all the forms of early tuberculosis mentioned above, the *ophthalmo-tuberculin reaction* is a great help in arriving at a decision.

In *pulmonary tuberculosis with demonstrable local lesion*, the diagnosis is easier. The patients now have cough, dyspnea, pains in the chest, and sometimes hemoptysis.

The *cough* may be a "dry cough," characterized by its short, non-resonant sound and by the absence of sputum, and of râles; it is usually worse at night. In another form of cough, there is associated vomiting of unaltered food. These two forms of cough are sometimes supposed to be "nervous cough." The patients are often hoarse. In a third form of cough, the so-called "catarrhal cough," there is mucous expectoration, sometimes tinged with blood.

Not so much stress can be laid upon *dyspnea*, or upon *pains in the chest*, as signs of tuberculosis, since they occur in the most different varieties of intrathoracic disease.

Hemoptysis may be the first symptom of incipient pulmonary tuberculosis, and it may recur at different stages of the process. Hemoptysis alone does not permit of the diagnosis of pulmonary tuberculosis, however, since it may occur in bronchiectasis, in neoplasm, in lung syphilis, in cardiac disease, in aortic aneurism, in throat affections, in vicarious menstruation, etc.; but if hemoptysis be associated with other signs of tuberculosis, or occur in persons with the habitus phthisicus, or with a tuberculous family history, it speaks strongly in favor of a tuberculous infection. It may or may not be associated with fever.

Whenever there is any *sputum* in a patient with signs suggestive of tuberculosis, it should be repeatedly examined by the *Ziehl-Neelsen method* for tubercle bacilli. If persistently negative by this method, it may be examined by the *antiformin method,* or be sent to a laboratory with the request that a *guinea-pig be inoculated.*

ii. General Remarks on the Early Diagnosis of Tuberculosis in Children

Von Behring (1903) believed that the pulmonary tuberculosis of adults is simply "the end of a song which was sung by a candidate for tuberculosis when in the cradle." In other words, he believes that tuberculous infection occurs during the suckling period, through milk.

The introduction of von Pirquet's test and of the ophthalmo-reaction for the study of tuberculosis in children has, as a matter of fact, opened our eyes to the frequency of childhood infection, and the clinical findings have been confirmed by the pathological anatomists.

At present, the supporters of two views are fighting for ascendency regarding the mode of infection: (1) that of *aërogenous* infection and (2) that of *enterogenous* or alimentary infection. While *congenital* infection may occur, it is now generally considered that it plays but little, if any, rôle in the origin of human tuberculosis.

There can be no doubt that *children become infected from some human being* (phthisical father, mother, sib, servant, playmate, neighbor) who distributes bacilli in their neighborhood. The younger the child, the greater the danger of infection; hence, in taking the family history, it is very important to inquire into the associates of the infant up to the time it was two years old (Hamburger). After infancy, the child may be exposed at the kindergarten or in the schools.

Judging by tuberculin tests of children between 7 and 10 years of age, 64 per cent yield a positive reaction; between 11 and 14 years, 77 per cent. It seems therefore probable that the majority of children, especially among the poor, are *infected* with tuberculosis, though not *sick* with tuberculosis. According to Naegeli, 97 per cent of the individuals coming to autopsy in Zurich show the signs of a healed tuberculosis. In other words, *practically every human being is at some time or another infected with tuberculosis.*

It would seem that the disposition to tuberculous infection is very pronounced in the suckling period, and less pronounced later on.

It goes without saying that *material and social factors* are of great importance in diminishing, or in increasing the disposition to tuberculosis; children who are abundantly nourished, and who live in favorable hygienic surroundings, are far less predisposed to tuberculosis than the poor.

Of the diseases of childhood which increase the disposition to tuberculous disease, *measles* and *whooping-cough* occupy the first place.

Children with *exudative diathesis* (Czerny) possess a peculiar predisposition to scrofulosis or tuberculosis of the lymph glands.

The *course of tuberculosis in children* varies much in different instances, depending (1) upon disposition, as above discussed, (2) on the grade of infection, and (3) on the age of the child. The differences in the manifestations of the disease in children from those in adults is explained by the lower capacity for resistance in the infantile organism, the tissues having very little tendency to localize or to heal tuberculous processes. It is therefore common to find a *generalization* of the process in young children. The bacilli invade a whole series of organs (lymph glands, spleen, kidney, liver, bones, etc.). The *predilection site* of infantile tuberculosis is, however, the bronchial lymph glands, and it is thence that the other organs, like the lungs, spleen, bones, joints and brain, most often become infected. This is in marked contrast with what is met with in adults, in whom the predilection site is the apex of one lung. As children approach puberty, the tendency to the adult form of localization of the tuberculous process begins to appear.

Rapid generalization of the tuberculous process with fatal termination is characteristic of the *first year of life* (Engel). In children attacked at this age, we observe a general nutritional disturbance, often otorrhea, eczema of the head, swelling of the lymph glands, tuberculous abscesses in the subcutaneous tissue and in the lungs, signs of a diffuse bronchial catarrh, or of bronchopneumonic foci in the lower lobes, with irregular fever and digestive disturbances. Every practitioner has been surprised to see a small child, apparently fairly healthy, suddenly attacked by a fatal tuberculous meningitis. During the suckling period, tuberculosis, once well started, runs a stormy course, always terminating fatally, usually with a picture of general miliary tuberculosis.

In *older children,* tuberculosis is less malign; there is less tendency to generalization, and an increased tendency to localization in certain organs, especially the bronchial lymph glands, the other lymph glands, the bones and the joints.

Pathological-histological studies of tuberculosis in childhood indicate that the tubercle bacillus, on entrance, may or may not at once produce tuberculous disease. In the latter case, it may remain latent, without undergoing multiplication, at some spot in the body, and cause no signs of disease (so-called *latent stage*). Later, under the influence of trauma or of some infection (measles, whooping-cough, influenza), the *latent tuberculosis* is transformed into a *manifest tuberculosis;* the tuberculosis spreads, (1) directly, by continuity, or (2) by carriage in secretions or excretions, as when the bladder becomes tuberculous secondary to tuberculosis of the kidney, or (3) through the lymph channels, or the blood vessels.

When *acute miliary tuberculosis* appears in childhood it presents the features of an acute infectious disease, usually beginning suddenly, with

quick rise of temperature, irregular pulse, dyspnea, cyanosis, usually dry cough, enlargement of the spleen, and marked cerebral symptoms due to miliary tubercles in the meninges. There may be no bacilli in the sputum or in the urine; sometimes bacilli will be found in the cerebrospinal fluid on lumbar puncture, or, on ophthalmoscopic examination choroidal tubercles may be visible. The disease is often confused with typhoid fever, with cryptogenetic sepsis, with capillary bronchitis, or with influenza.

In the *bronchial-gland tuberculosis* of children, the onset of the disease is usually insidious, with loss of appetite, pallor, emaciation, and slight atypical pyrexia; sometimes, the disease sets in acutely, with high fever and rapid emaciation. In s , the absence of outspoken objective signs elsewhere in the bod make one very suspicious of the existence of bronchial-gland uiosis. Two symptoms are, however, usually present to facilitate gnosis, namely: (1) a *high-pitched cough* and (2) an *expirator* ɔnea, both of which are the result of a compression of the bronchi ae swollen glands. These symptoms, will often permit of a positive d iosis, even at a stage when the children are still well nourished. S metimes the cough is more like that of whooping-cough, in which ca e it is probably due to vagal irritation. A *tuberculin test*, however, wil often distinguish between whooping-cough and tuberculosis.

The course of bronchial- gland tuberculosis varies much in different cases. It may be benign, becoming stationary through encapsulation of the focus and calcification of the glands. In malign cases, it extends from the lymph glands through the lymph vessels or the blood vessels, and gives rise to an acute general miliary tuberculosis. Sometimes a bronchial-gland tuberculosis that has long been stationary (encapsulation, calcification) is lighted up again by trauma, measles, or whooping-cough, and gives rise to an acute diffuse process. In the more advanced cases, röntgenography is very helpful in differential diagnosis, but it is desirable to make the diagnosis at an earlier stage.

In *early pulmonary tuberculosis in children*, the disease may take the form either of tuberculous pneumonia, or of chronic ulcerative tuberculosis (phthisis).

Tuberculous pneumonia in children is usually secondary, representing an acute process following upon a disease previously chronic. The clinical signs resemble those of a catarrhal, or of a lobar, pneumonia; longed beyond the period characteristic of benign . The nature of the process may be entirely obscure -nce of tuberculosis in the child, the family history, of the pneumonic process, and the presence of sputum clear up the diagnosis.

tuberculosis, like that of adults, is not very before puberty, though it may occasionally appear

after the 4th or 5th year of life. At the beginning, the little patient ceases to gain in weight, grows pale, emaciates, tires easily, and becomes irritable and capricious. A morning cough appears, though there may be no sputum at first. At the beginning the physical examination of the lungs may be negative, though later on small foci of infiltration appear. It is important to remember that in children with the signs of pulmonary tuberculosis we must direct our attention to the lower lobes of the lungs rather than to the apices; though, as children approach the age of puberty, the tendency to an apical localization becomes manifest, just as in adults. As the disease advances, röntgenoscopy, and especially stereoscopic röntgenography, afford important help in diagnosis. At this time outspoken infiltrations become demonstrable, and, later on, cavity formation and the signs of mixed infection with pyogenic cocci (hectic fever, profound emaciation) are met with.

Among the complications of pulmonary tuberculosis in children, *tuberculous pleuritis, laryngeal tuberculosis*, and *tuberculous ulceration of the intestines* are common, while hemoptysis is rare.

A systematic procedure should be followed for purposes of diagnosis when one suspects a beginning pulmonary tuberculosis in childhood. The regular routine should include: (1) a carefully taken anamnesis, (2) repeated precise examinations of the lungs, (3) the keeping of a two-hourly temperature chart for two weeks, (4) the keeping of a body-weight chart, (5) frequent examinations of the sputum (microscopically, and by animal inoculation), (6) cautiously undertaken tuberculin tests during afebrile periods, (7) stereoscopic röntgenography.

It is important, further, that the practitioner should be more or less familiar with the local lesions of the skin that occur in tuberculosis in childhood. These include (1) the tuberculids and (2) the scrofulids (Hamburger, Escherich).

Among the TUBERCULIDS may be mentioned: (a) *Gumma scrofulosorum*, in which there are indolent subcutaneous infiltrations of the skin of firm consistence, varying in size from that of a hemp-seed to that of a small cherry, often showing through the skin as bluish red nodules. They are sometimes attached to the skin and may, after softening, break through to the outside. They are most common in the lower extremities. In number, there may be only a single nodule taken by the family to be a boil, but in furunculosis there are usually many nodules, whereas a small number speaks in favor of gumma scrofulosorum. (b) *Lichen scrofulosorum*, with small lesions about the size of grains of wheat, or smaller, arranged in groups; they are of a bluish red color, or may be pale grayish white. They occur most commonly on the lateral part of the trunk. (c) The *tuberculids proper* include the papulosquamous and the papulonecrotic tuberculids. All these varieties follow a very chronic course and, on account of the scanty number of the lesions, must be sought for if they are to be observed.

Among the SCROFULIDS may be mentioned: (a) *Phlyctenular conjunctivitis*, sometimes called conjunctival tuberculids. These are small, scarcely visible, grayish white nodules in the conjunctiva. They are surrounded by a markedly hyperemic

zone. On superficial examination, the process may be taken to be a simple form of conjunctivitis with photophobia. (b) *Chronic blepharitis.* (c) *Scrofulous rhinitis.* (d) *Thickening of the upper lip.* (e) *Moist eczema.* (f) *Catarrhal inflammations* of the throat, ear, air passages and digestive tract. (g) Multiple *indolent enlargements of the lymph glands.*

In all these children with signs of scrofulosis, a positive tuberculin reaction can be obtained. In other words, scrofulosis falls within the domain of tuberculosis.

One must differentiate these scrofulous lesions, especially those involving the lymph glands, from (1) Pfeiffer's *glandular fever,* (2) Schick's *postscarlatinal lymphadenitis,* and (3) *lymphadenoid leukemia* and *aleukemic lymphadenosis.*

The diagnosis of *tuberculous serositis* and of *tuberculous meningitis* is described elsewhere, as are the methods of using the tuberculin tests, and of making x-ray examinations in tuberculosis of the lungs and of the bronchial glands. Here, however, may be mentioned the *contra-indications to a diagnostic tuberculin test*: (1) In cases in which the clinical diagnosis is clear, especially when tubercle bacilli are present in the sputum or urine, a tuberculin test is superfluous. (2) In advanced infiltrative processes in the lung, a tuberculin test need not be made. (3) In cases in which the mouth temperature is above 37° C., a tuberculin test should not be made. (4) During hemoptysis, and for a short time after, the test should be avoided. (5) In outspoken nephropathy, no tuberculin test should be made. (6) In very neurotic patients, a positive tuberculin test is of doubtful value, owing to the fact that such patients often react with fever to a hypodermic injection even of water. (7) In epileptic patients, a tuberculin test may call forth an attack. (8) In suspected tuberculosis along with severe constitutional disease (diabetes mellitus, typhoid fever, pneumonia) it is best to avoid a diagnostic tuberculin test.

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19. Diseases Due to the Leprosy Bacillus

Leprosy Bacillus.—The *Bacillus lepræ* (Hansen, 1872), studied carefully by Neisser (1879), is a slender, non-motile, acid-fast, rod, 4-6 μ long by 0.3-0.5 μ broad, present in *enormous* numbers inside the cells, or within the lymph spaces of the lesion. Both ends of the bacilli are often pointed. The bacilli show a strong tendency to grow in masses, in which the individual bacilli are parallel to one another—so-called *cigar-bundle masses* of bacilli—or *glœa* of Unna, or *globi*. Many of these lepra-globi are bacillary thrombi in the lymph vessels. On staining by Gram's method, each bacillus is seen to contain rows of granules (Lutz and Unna); they correspond to the Babes-Ernst granules of other bacteria. Many of the granular forms will not stain at all in carbol-fuchsin, but are beautifully demonstrable by Much's modification of the Gram stain. *Diphtherioid, partially acid-fast bacilli* have occasionally been grown from leprous lesions (Bordoni-Uffreduzzi, 1886; Babes, 1901; Duval; and Kedrowsky). According to Keitschewsky and Bierger (1913), complement-fixation tests indicate that Kedrowsky's strain is identical with Hansen's bacillus, and Duval's is not. *Acid-fast streptothrix forms* have been grown from leprous lesions by several observers (G. Deycke, 1903; Williams, 1911; Bayon, 1912). Thus far, the actual proof of a causal relationship between either the diphtherioid bacilli, or the streptothrix forms, has not been brought forward. (Plate IV, Fig. 1.)

Experimental Leprosy.—Attempts to produce leprosy in experimental animals have been made by many workers (Melcher and Ortmann, 1885;

Kedrowsky; Bayon; Nicolle; Much), but have not been satisfactory. Attempts to inoculate healthy human beings have also been made (Daniellsen and Boeck), but have failed, except in the single instance of the criminal Keanu, condemned to death in Hawaii, but pardoned on condition that he would submit to inoculation of leprous material as a scientific experiment. He was inoculated by Arning and two years later was manifestly leprous, but as certain distant relatives were leprous, the case is not wholly free from objection.

In infected human beings, leprosy bacilli are almost always present in the nasal secretions (Sticker). They are sometimes present in the saliva, in the sputum, in the milk, in the feces, and in the blood.

In about 70 per cent of the cases of the tuberous form of leprosy, the Wassermann reaction is positive (Meier), and complement fixation for tuberculin is said to be positive in a very large percentage. Möllers (1913), out of 32 sera, from 20 patients with tuberous, 8 with nervous, and 4 with mixed lepra found complement-binding antibodies to tuberculin preparations in no less than 25. This probably points to a "group-reaction," due to the biological relationships of the bacilli of leprosy and the bacilli of tuberculosis.

(*a*) *Human Leprosy* (*Lepra*)

Epidemiology.—The disease is transferred directly from the patient to other human beings, though the degree of contagiosity must be very low and the possibility of an intermediate change in the virus has to be considered. Just how the transmission occurs is disputed. Close relationship, as in families and sleeping in the same bed, or sexual intercourse, seem to be responsible, and, recently, Honeij and Parker have shown that a species of fly (*Stomoxys calcitrans*) may carry the bacillus. Insects, however, play no part in the actual transfer of the disease, as far as is known. The *anesthetic form* is but little, if at all, contagious. The *tuberous form* is the most dangerous, probably because the patients give off bacilli on coughing, or through open wounds.

Congenital infection is exceedingly uncommon. The Commission of the National Leprosy Fund in India collected 1,564 instances of leprous parents who had 2,915 children, of whom only 75 had leprosy. Sand (1910), in Norway, reported 512 leprous parents with 1,835 children, of whom 1,710 (93.2 per cent) were healthy, and 125 (6.8 per cent) were leprous. In 17 instances, both parents were leprous and had 55 children, of whom 8 (i. e., 12.7 per cent) were leprous.

The disease is very widely distributed over the earth's surface. Fortunately, the northern parts of America are relatively free from the disease; autochthonous leprosy does not occur in Canada, nor in the United States, except perhaps in Minnesota and in Louisiana. In Mexico, Central America, and the West Indies, the disease is common; about 1 in

every 1,000 of the population is affected. The countries in the northern part of South America suffer still more. In Colombia there are over 4,000 lepers (Montaya y Florez); in British Guiana, 1 out of every 250 or 300 of the population has leprosy (Hillis; Deycke). Brazil and Argentina are less affected; Chili is relatively free from the disease. The nodular form is most common in countries in which the disease has been newly introduced, the nervous form in countries in which the disease has long existed. The disease is widespread in Asia, Africa, and certain parts of Europe.

Symptoms.—The incubation period is very long, 3-5-10-20 years elapsing after exposure before symptoms develop. In the early stages, subjective disturbances of sensation (hyperesthesia, itching, formication) are common; other early signs include falling out of the hair, dry rhinitis with epistaxis, and hypersecretion of sweat and of sebum. The first visible signs of general infection are skin lesions (maculae, vesicles, nodules). The mucous membranes of the larynx and of the nose may be early infected.

Three principal clinical forms are distinguished: (1) nodular, or tubercular, leprosy (*lepra nodosa*), (2) nervous, or anesthetic, leprosy (*lepra nervorum*), (3) mixed leprosy (*lepra mixta*). There would seem to be no good reason to set up a paralepra, analogous to paralues, as Zambaco has attempted to do.

i. Lepra nodosa (Lepra tuberosa)

The characteristic nodules appear in the skin, usually on the extensor surfaces of the extremities, sometimes symmetrically arranged; they are not rare on the face and back. The color is at first carmine red; the center gradually grows darker, becoming brown or brownish-red. The hairs fall out and the skin becomes infiltrated. The face is usually involved and ulcers and cicatrization follow, the face assuming a peculiar appearance (*facies leontina*), in which there is loss of skin pigment, and loss of the eyebrows, eyelashes, and beard.

ii. Lepra nervorum

Here the sensory and trophic disturbances due to disease of the peripheral nerves are most marked, but there are also leprous changes in the skin, mucous membranes, and internal organs. The onset is insidious, with erythemas and macular eruptions (symmetrical). There may be pains or cutaneous hyperesthesia at first. The thickened nerves can be felt through the skin in both lepra nodosa and lepra nervorum, especially the *nervus auricularis magnus* in the neck. I palpated this nerve in a number of lepers in the Philippine Islands and was surprised to find how frequently it was thickened. The N. ulnaris is also often palpable, but since

this can often be felt in normal persons, palpation of this nerve is less helpful in diagnosis. Islands of anesthesia develop; sometimes the anesthesias are widespread.

On röntgenography, the trophic lesions in the bones, especially of the

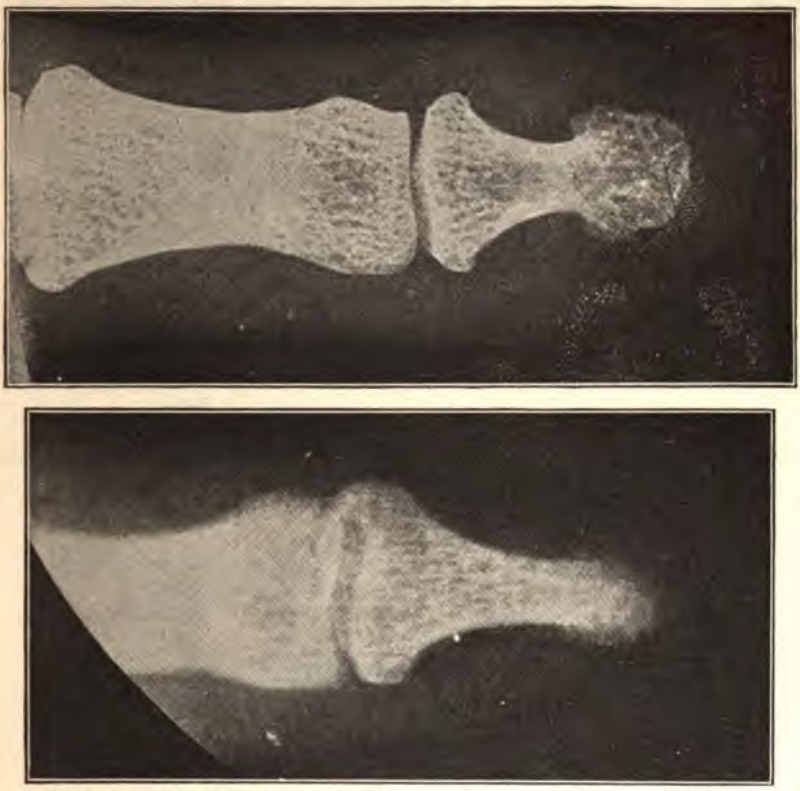

Fig. 84.—Middle and Distal Phalanges of a Normal Finger Compared with Those of a Case of Leprosy. Note in Diseased Finger Beginning Absorption of Bulbous Tip of the Distal Phalanx, and an Associated Narrowing of Shaft. (After A. B. Herrick and T. W. Earhart, Arch. Int. Med.)

fingers may be pronounced; in Tokio, in 1899, K. Miura showed me interesting negatives illustrating these changes.

iii. Lepra mixta

Most cases of leprosy are more or less "mixed," but usually the nodular, or nervous, lesions markedly predominate. In some cases, they appear in about equal numbers.

Complications of Leprosy.—Pyogenic infections; carcinoma.

Diagnosis.—If leprosy be suspected, the signs are usually so distinct, or the bacilli can be so easily demonstrated in the lesions (carbol-fuchsin method, or, better, Much's modification of Gram's method), that doubt is soon dissipated. This is especially true of the tuberous form; the

ous fuchsin solution); it is Gram-negative. Aërobic cultures alkaline agar grow best at 37° C. The bacillus liquefies el-formation), peptonizes blood serum and forms indol in ons ("cholera red reaction"). The bacillus is extremely ry heat, and to disinfectants. Its virulence is variable. cted in the ear vein, develop diarrhea and die. Accidental h pure cultures of cholera bacilli have occurred in human atory infection). Prof. Pettenkofer of Munich, who denied f the bacillus to the disease, intentionally swallowed a cholera making the stomach juice alkaline with bicarbonate of soda. d cholera, but recovered. Prof. Emmerich is also said to have culture, along with an excess of beer, and he, too, had a severe pical Asiatic cholera as a result. (Plate IV, Fig. 3.)

(*a*) *Asiatic Cholera*

on.—An acute infection of the surface of the intestine, due to *oleræ asiaticæ* (Koch) and characterized by violent purging collapse.

iology.—The disease occurs (1) in *great epidemics* breaking ly (water-borne infection), and (2) *sporadically* (contact infec- lus carriers).

oms.—There may be slight premonitory symptoms (diarrhea, pains, headache, malaise); more often, there is a sudden attack, ing and profuse diarrhea; the diarrheal defecation is painless. ischarges, at first feculent, soon become watery, colorless, and the so-called *rice-water stools*—and contain the comma bacilli umbers with flecks of mucus, detritus and sometimes blood. rostration quickly follows, with small rapid pulse, cyanosis, and mities (*stadium algidum*). Nothing can be retained in the here is boat-shaped retraction of the abdomen; the voice becomes hoarse (*vox cholerica*); the tissues are dehydrated, the skin ıkled, dry and devoid of elasticity, and the urine scanty or ramps in the calves of the legs develop. Though the extremities ment may feel cold to the touch the rectal temperature is usually Death may ensue in a few hours.

der cases, the symptoms gradually decrease, the skin becoming moist (*stadium reactionis*). The kidneys begin to secrete again, containing albumin and casts.

es are not uncommon, the extremities becoming again cold and the patient feeble and apathetic, with renewal of the fever, nd muscular cramps. The diarrhea and vomiting recur, and the ıks into coma (*stadium comatosum*, or *cholera typhoid*), which ds fatally, though occasionally a patient recovers.

algid stage, the leukocytes may number over 40,000, owing

to concentration of the blood; during the stage of reaction, they rapidly decrease in number.

Sellards has shown that a marked acidosis accompanies the dehydration in cholera, and constitutes one of the dangerous features of the disease.

When the attack is not severe, but resembles an ordinary catarrhal gastro-enteritis, even though comma bacilli are demonstrable, the condition is known as *cholerine.*

The average mortality in Asiatic cholera is 50 per cent to 60 per cent; the death-rate varies in different epidemics.

Diagnosis.—It is all important to recognize the first cases, which must be differentiated from (1) *cholera nostras,* or *paratyphoid infection,* and (2) *arsenical poisoning.*

Where cholera is suspected, an expert bacteriologist should make a systematic examination of a particle of mucus from the feces, or from the vomitus: (1) Microscopically (many vibrios in smears stained in carbol-fuchsin; motility in hanging-drop, in peptone solution); (2) By cultural methods (gelatin and agar plates, after enrichment by planting an oese of the mucus in several tubes of Schottmüller's slightly alkaline, salt- and nitrite-containing peptone solution, and incubating at 37° C. for 6 hours, when enormous numbers of vibrios owing to their affinity for oxygen will have accumulated near the surface of the medium; from this surface layer, plate cultures on gelatin, on agar and on Dieudonné's blood-alkali agar are made); (3) By testing pure cultures (a) for agglutination with immune serum, (b) by Pfeiffer's experiment (q. v.) and (c) for the nitroso-indol-reaction (red color on addition of H_2SO_4 to the growth in nitrite-containing peptone water).

Special *cholera courses* should be given in the bacteriological laboratories at the time of cholera epidemics, so that the local health officers can learn to act promptly and with certainty.

Prophylaxis.—All water used in times of cholera should be boiled and no uncooked food should be eaten. Great care should be taken to avoid dietetic errors. Every digestive disturbance should be met promptly (rest in bed; bismuth). All suspects should be isolated. The drinking of acidulated water (lime juice, citric acid, muriatic acid) is recommended.

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21. Disease Due to the Bacillus of Milk Sickness

Bacillus of Milk Sickness.—The *Bacillus lactomorbi* (Jordan and Harris) was isolated from cases of milk sickness in an epidemic in New Mexico (1908), and grown in pure culture. Inoculation of animals with the culture reproduces the disease.

(*a*) *Milk Sickness*

Symptoms.—The symptoms consist of nausea, vomiting, intense thirst, fever, and abdominal pains, with constipation. The breath is foul, the tongue swollen and tremulous; mental symptoms are often marked. Death may occur in from 3 to 21 days.

In cattle, the disease known as the *trembles* appears to have the same etiology. Man is presumably infected through meat, milk, butter or cheese.

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22. Disease Due to the Bacillus proteus vulgaris

Bacillus proteus vulgaris.—This bacillus has been isolated from the liver, and from the kidney, in cases of acute infectious jaundice, sometimes known as *epidemic catarrhal jaundice* or WEIL'S DISEASE. A similar disease is often due to infection with the paratyphoid bacillus. (See Part VIII.)

23. Diseases Due to Bacillus typhi-exanthematici

(*a*) *Typhus Fever*

(*Typhus exanthematicus, Spotted Fever, Camp Fever, Brill's Disease*)

Definition.—Typhus fever is an acute, specific, febrile, infectious disease, with characteristic macular, often hemorrhagic, exanthem, and accompanied by severe nervous and mental symptoms, occurring generally in epidemics, though occasionally sporadically; it was definitely differentiated from typhoid fever by Gerhard (1829).

Occurrence.—Formerly the disease was very prevalent; now it is rare, except in countries or in communities in which there are notoriously bad hygienic conditions. In 1815-1818, the disease was epidemic in England and Ireland; one-eighth of the Irish population died of it. In 1846-1848 over a million people in England suffered from the disease. In the Russo-Turkish war (1877-78), no less than 32,451 Russian soldiers died of typhus exanthematicus. The disease still occurs, occasionally in epidemics, and sporadically, in different parts of the United States and Europe. Thus the fever, not uncommon in New York, and known as Brill's disease, has been shown to be typhus fever (Anderson and Goldberger), as has also the tabardillo of Mexico. A young scientist, Dr. H. T. Ricketts of Chicago, died from this disease, contracted while investigating it in Mexico.

Etiology.—The nature of the virus was, until recently, unknown, though it is present in the blood during the febrile stage, and can be transmitted, by blood inoculations, to monkeys and to guinea-pigs. The virus does not lose virulence on heating for 15 minutes at 55° C. One attack of the disease appears to yield permanent immunity.

Ricketts and Wilder were the first to show that the disease could be

transmitted by the bite of the louse. On this discovery are based all the prophylactic measures that are now so successfully used.

The disease can be transmitted from man to man by the body-louse (*Pediculus vestimenti*), and by the head-louse (*Pediculus capitis*), which probably explains its prevalence in epidemic form in over-crowded, filthy surroundings ("camp fever"). Lousiness, formerly common, is rapidly disappearing; the same is true of typhus fever. The most cleanly or fastidious person, compelled to work in certain surroundings, may occasionally be bitten by lice, and if the lice carry the virus, contract the disease.

Recently, Plotz, Olitsky and Baehr have reported the discovery of *B. typhi-exanthematici* as the cause of typhus fever. The organism was recovered from the blood of several cases of European epidemic typhus fever and also from cases of the mild endemic form of the disease known in the United States as Brill's disease. Moczutkowski had proved that the virus is present in the circulating blood during the febrile period; he inoculated himself with blood from a typhus patient, and typical symptoms of the disease developed at the end of an incubation period of eighteen days. Nicolle (1909), by injecting the blood of patients into chimpanzees, reproduced the disease. He was able to transmit the disease from monkey to monkey by the bite of the body-louse. The studies of Nicolle, of Ricketts and Wilder, and of Anderson and Goldberger, had shown that the virus is non-filtrable. Ricketts and Wilder then pointed out that typhus fever is an acute, self-limited disease, one attack of which confers immunity, and they emphasized the fact that these features favor a bacterial rather than a protozoal origin.

A B

Fig. 85.—(A) Tube Showing Growth (Seven Days) of Bacillus typhi-exanthematic on Serum Glucose Agar. Note Whitening of Medium (Precipitation). (B) Control Tube of Glucose Serum Agar. (After Plotz, Olitsky and Baehr, J. of Inf. Dis.)

Cultures made by aërobic methods by many investigators have been negative. In 1914, Plotz, under Libman's direction, first isolated a bacillus by anaërobic methods. He used first Noguchi's method for the cultivation of spirochaetes, but later found the Liborius-Veillon method more satisfactory. Colonies of the bacillus appear in the tubes in from three to sixteen days. "The organism is a small, pleomorphic, Gram-positive bacillus, not motile, not encapsulated, and not acid-fast. Its length varies from 0.9 to 1.93 μ, its breadth being from one-fifth to three-fifths its length." It does not produce spores. It is an obligatory an-

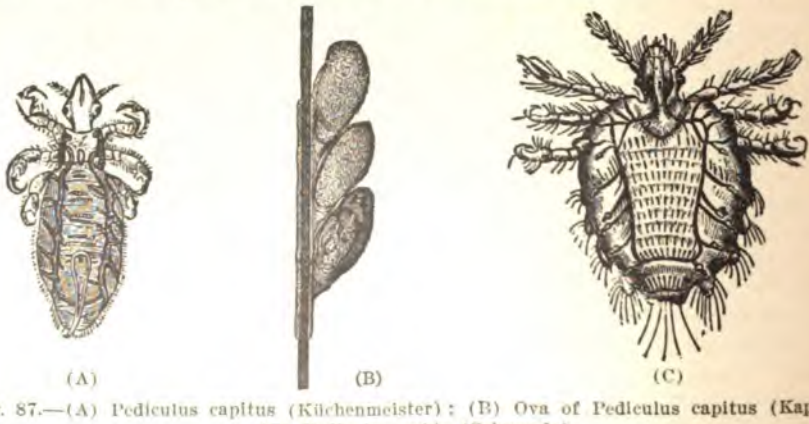
aërobe. The bacteriemia is more marked in the epidemic than in the endemic cases. Owing to the slow development of the colonies in the culture media, the results of the blood cultures are, as a rule, not determinable, until after the end of the illness, but it is maintained that the cultures are of value for confirming the clinical diagnosis. Plotz reports that, in 87.5 per cent of 51 cases studied, the clinical diagnosis was confirmed by blood culture, agglutination or complement-fixation tests. In two cases in which the diagnosis had been overlooked, a positive blood culture first called attention to the nature of the condition.

Fig. 86.—Bacillus typhi-exanthematici—Gram's Stain. x 1,000. (After Plotz, Olitsky and Baehr, J. of Inf. Dis.)

It is asserted that the disease can be typically reproduced in animals by inoculation with pure cultures of the bacillus, and that from these animals the identical organism can be recovered from the circulating blood.

Olitsky, who made the immunological studies, found that complement-fixing antibodies against the bacillus occur in typhus fever, and not in other conditions. Specific agglutinins, specific precipitins and specific immune opsonins are also present, but specific bacteriolysins or bacteriocidins are not demonstrable. The results of further studies upon this bacillus will be awaited with interest. In personal communications from Serbia, I am told that investigators there have thus far had difficulty in confirming the findings of Plotz, Olitsky and Baehr.

Prophylaxis.—This consists chiefly in a campaign against lice. If contaminated clothing be soaked in a 1:500 solution of bichloride of mercury,



(A) (B) (C)

Fig. 87.—(A) Pediculus capitus (Küchenmeister); (B) Ova of Pediculus capitus (Kaposi) (C) Pediculus pubis (Schmarda).

the lice and their eggs will be destroyed. After closely clipping the patient's hair, the head should be thoroughly sponged in bichloride solution (1:2,000) to destroy lice eggs. The lice in a bedroom can be killed by sulphur fumigation. Doctors and nurses attending typhus patients should take especial care to avoid louse bites. Many distinguished members of both professions have succumbed to typhus fever, contracted at the bedside. According to Osler, "in a period of 25 years in Ireland, among 1,230 attached to institutions, 550 died of this disease."

Symptoms.—The incubation period lasts from 5 to 20 days, averaging 12 days. The onset is usually sudden, with chill, or chills, and fever, headache, severe prostration, pain in the back and legs, tachycardia, coated tongue, suffusion of the face and eyes, mental dullness, often delirium, and vomiting.

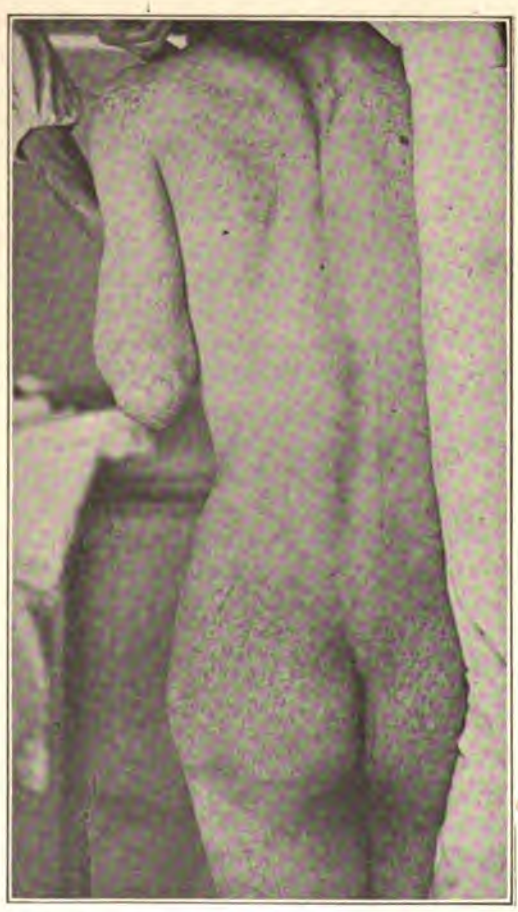


Fig. 88.—Typhus exanthematicus. (Med. Service, J. H. H.)

The exanthem appears on the 4th and 5th day, first upon the lower abdomen and the shoulders, later upon the back, chest and upper abdomen, and lastly upon the face and extremities, the whole rash appearing within 2 or 3 days; it lasts a few days, in the severer cases for a week or longer. The rash consists of pale red spots the size of a pin's head, or of a pea (macular, not papular); in a few days it assumes a dirty red or copper-colored tint and ceases to disappear on pressure; some of the spots become definitely hemorrhagic (petechial). The spots are often very abundant in the inguinal regions. In addition, there is usually a dusky red, subcuticular mottling.

In the cases known as Brill's disease, the rash may resemble the rose spots of typhoid fever, or may be absent altogether. Toward the close of the first week and during the second week, the symptoms are more

pronounced, especially the fever, prostration, the delirium and stupor. Urinary retention and coma-vigil are common. The tachycardia and tachypnea are marked.

The *fever*, in contrast with that of typhoid, rises suddenly, rather than by steplike ascent. The remissions during the first week are slight (about half a degree). Defervescence occurs about the end of the second or beginning of the third week either by crisis, or by rather rapid lysis, the fall being often preceded by a critical perturbation, or by a pseudo-crisis. Instead of the slow lytic fall seen in typhoid fever, the fall of the temperature in typhus exanthematicus occurs within 12-24 hours to subnormal. Hyperpyrexia is not rare.

The blood usually shows a slight leukocytosis (12,000-15,000), with a relative increase in the lymphocytes; in severe cases, anemia may develop rapidly in the later stages.

The spleen is occasionally palpable at first, but diminishes in size during the fever. The urine is scanty and contains a trace of albumin; the diazo-reaction is positive. Blood cultures made in the ordinary aërobic way and Widal reactions are negative. Bronchopneumonia is the commonest complication met with.

Diagnosis.—The very sudden onset, the course of the fever and of the pulse and the appearance of the exanthem make the diagnosis easy at times of epidemic. Sporadic cases are often wrongly diagnosed.

The disease should be differentiated: (1) From *typhoid fever* (positive blood culture in the first week, leukopenia, rose-spots and their distribution, palpable spleen, dicrotic pulse, more insidious onset, longer course, Austrian's ophthalmic test). (2) From *smallpox* (eruption different in character with definite cycle of evolution, the distribution of the initial exanthem, the fall of temperature before the outbreak of the main exanthem). In purpura variolosa, the differentiation in a sporadic case from typhus exanthematicus may be impossible, though subsequently the corneal experiment (q. v.) may reveal the true nature of the case. (3) From *malaria* (intermittent fever, parasites in the blood, leukopenia, large firm spleen). (4) From *relapsing fever* (blood examination). (5) From *sepsis with hemorrhagic eruption* (leukocytosis, cocci in blood culture, primary focus). A most useful diagnostic test in doubtful cases is the *test of Anderson and Goldberger* (injection of patient's blood into peritoneal cavity of guinea-pig; if the disease be typhus exanthematicus, or Brill's disease, a typical temperature curve will be obtained).

From now on anaërobic cultures by Plotz's method should be undertaken when the disease is suspected to exist.

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C. Diseases Due to the Coarser Fungi (The Mycoses)

Formerly, only actinomycosis and thrush were adequately described in text-books of internal medicine. In recent years, a whole series of diseases, due to different kinds of fungi, have become recognized and the chapter on the mycoses is one of the most interesting in internal medicine. It is a worthy field, also, to work in, since the early recognition of certain forms, especially of the sporotrichoses, permits of the rapid cure of a disease that otherwise may be very serious. Many of the mycoses stand in the borderland between internal medicine and surgery. Like so many borderland diseases, they are apt to be neglected. For this reason, I am dealing more fully with them than is perhaps customary.

Definition.—The mycoses include a group of external and internal diseases of human beings and animals, due to the coarser forms of parasitic fungi, thus differing from forms of infectious disease due to bacteria or to protozoa.

Varieties of Mycoses.—Among these mycoses, we include the diseases due to (1) ordinary HYPHOMYCETES (mucor, aspergillus, penicillium, achorion, trichophyton, etc.), in which a genuine mycelium is formed and which propagate by spore formation, or by the production of higher forms of fructification organs; (2) the BLASTOMYCETES or yeast fungi, which multiply by budding and by spore formation (saccharomyces, yeasts), and only exceptionally give rise to mycelium (blastomyces, oidiomyces, thrush fungi, etc.), and, finally, (3) the STREPTOTHRICES, which consist of branched threads, breaking up into short rods, and propagate by fission (streptothrix actinomyces, streptothrix of madura foot, nocardia forms, leptothrix, etc.).

These different varieties of the coarser fungi are not yet entirely satisfactorily placed from the botanical standpoint, though the French in-

vestigators, especially, have gone far toward giving us a purely *botanical classification.* Thus, in the recent valuable volume on parasitic diseases in Gilbert and Thoinot separate chapters are devoted to (1) sporotrichoses, (2) botrytimycoses, (3) hemisporoses, (4) exascoses, (5) oidiomycoses, (6) mucormycoses, (7) oösporoses, (8) aspergilloses, and (9) actinomycoses.

Such a botanical classification, however, is, I fear, for practical purposes, a little premature, and, with Plaut, I am inclined to adopt a *simpler grouping,* as follows: (1) mycoses due to hyphomycetes, (2) mycoses due to blastomycetes, (3) mycoses due to thrush fungi, (4) mycoses due to sporotrichum and related fungi, (5) mycoses due to the different varieties of streptothrix (actinomyces, madura foot, nocardoses, leptotrichomycosis, etc.).

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1. Mycoses Due to the Hyphomycetes

Hyphomycetes.—These are fungi that form whitish, greenish, yellowish, brownish or blackish deposits on organic substances like fruit, bread, carpets, preserves, straw, manure, etc. Botanically, these hyphomycetes include several species (e. g., aspergillus, mucor, penicillium, botyris, achorion, tricophyton and microsporon). Many of them are pathogenic for man and for animals, the more important belonging to aspergillus and mucor.

Aspergillus belongs to the *mycomycetes,* sub-variety, *ascomycetes.* It is an asexual form of *eurotium,* in which the more complex form of fructification, known as ascus formation, occurs also. The conidiophore is strong, and presents a flask-like swelling at its end, upon which sit short, wedge-like pedicles, the so-called sterigmata, in stellate arrangement. From these sterigmata, the spores, or conidia, are pinched off in chains; the color of these varies according to the variety (black, yellow, etc.). The pathogenic varieties include (a) *Aspergillus fumigatus,* (b) *Aspergillus*

niger, (c) *Aspergillus flavus,* and (d) *Aspergillus nidulans.* Infections with aspergillus fumigatus are by far the most common.

In testing aspergillus for its pathogenicity, it is best to use guinea-pigs and birds. After intravenous injection of the spores, the animals die in from 48 to 72 hours.

Mucor belongs to the *phycomycetes,* or algae-fungi. Its mycelium is either free from septa, or poor in septa; it gives rise both to sexual and to asexual spores, which form in sporangia that rest upon conidiophores, easily distinguished from the rest of the mycelium by their length and thickness. During the spore formation, the conidiophore undergoes club-like swelling at its end, the septum immediately beneath giving rise to the so-called columella. The asexual spores are formed from the protoplasm that lies beneath the columella and the surface of the club. The whole structure is known as a sporangium. The membrane of the sporangium bursts when the spores are ripe and they are scattered through the air. Of the pathogenic forms, the commonest are (a) *Mucor corymbifer* (lung, ear); (b) *Mucor rhizopodiformis,* and (c) *Mucor septatus* (ear).

In testing the pathogenicity of a mucor, it is best to use rabbits (intravenous injection).

Penicillium is the commonest of all the hyphomycetes. It is the asexual form of an ascus-forming *perisporiacea.* Asci, however, are seldom seen. This fungus is distinguished from aspergillus by the fact that the conidiophore does not undergo bulbous enlargement and is subdivided at its apex. From the tips of these subdivisions, the sterigmata give off chains of spores by budding.

Pathogenic varieties have been found in the ear.

Fungi Affecting the Skin.—Here belong *Achorion schoenleinii* (favus), *Trichophyton* in its different forms, *Microsporon furfur* (of pityriasis), and *Microsporon minutissimum* (of erythrasma).

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(*a*) *Human Aspergillosis*

The infection is met with in diabetes and in cachexias. The fungus may invade the skin (*dermatomycosis*), the ear (*otomycosis*), the nose (*rhinomycosis,* the lungs (*pneumonomycosis aspergillina*). A very interesting case of the pulmonary form has been described by Osler. Persons exposed to vegetable dust (millers, gardeners) are frequently affected. In France, the so-called *pigeon-fancier's disease* or *pseudotuberculosis aspergillina* is due to aspergillus, the infected persons allowing the birds to take masticated food directly out of their mouths; these birds often suffer from spontaneous aspergillosis. Hair-sorters who comb out hair with the use of

meal containing fungi, and sponge-cleaners, through the dust from the dry sponges, may also contract the disease.

Pinta.—A parasitic skin affection found only in the tropical regions of the Western Hemisphere and characterized by the appearance of black, red, violet, and white patches on the skin. These patches have been shown to be due to various fungi, of which *Aspergillus pictor*, Penicillium montayai, Montoyella, and Monilia are the best known. The patches are usually first noted on the hands; itching is marked; and apparently by scratching the process is spread over the body. The diagnosis can be made from the examination of scrapings in liquor potassæ; and by the cultivation of the fungus on Sabouraud's medium.

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(*b*) *Human Mucormycoses*

Fungi belonging to mucor have been found in infections of the lung and of the ear; also in enteritis. In one case there was a generalization of infection from the intestinal lesions with multiple abscesses in the brain, lungs and elsewhere (*Mucor corymbifer*).

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(*c*) *Human Achorion-mycosis or Favus*

This is a disease of the hairy scalp, due to invasion by *Achorion schoenleinii*. The *Achorion schoenleinii* belongs to the hyphomycetes. It is rich in mycelium and shows only a few gonidia. A scraping, treated with NaOH, examined under a cover-slip shows it well. Yellowish, disklike scales (scutula) having a peculiar earthlike odor, and perforated in the middle by a hair, appear. If a scutulum be raised, one sees a red, moist surface underneath and in chronic cases atrophy of the underlying skin. Later, the encrusted areas enlarge and become confluent, forming thick, yellow encrusted areas. Suppuration is not uncommon at the edges of the lesions. The hairs are involved early, becoming dull, brittle and often splitting or falling out, so that one may find atrophic almost hairless areas, with crust formation at the borders.

In one case, reported by Kundrath, there was an intestinal favus and a general favus-sepsis!

The **diagnosis** is made by examining a scutulum, in NaOH, under the microscope, and looking for the typical fungus. The presence of this differentiates the disease from a seborrheic eczema resembling it.

(*d*) *Human Mycoses Due to Trichophyton tonsurans*

The *Trichophyton tonsurans* met with in the human skin is seen in delicate thread-forms in a mycelium, with roundish or oval gonidia, arranged usually in chains. The threads are often tortuous and curved, but rarely branched.

Scales, hairs and crusts containing the fungus, cleared in NaOH or KOH, reveal it distinctly, on microscopic examination, though sometimes a number of specimens must be examined before the fungus is found. It causes several different forms of disease in man.

i. Superficial Ringworm (Trichophytia superficialis)

This is an inflammation in the most superficial part of the skin, due to the lodging and growth of *Trichophyton tonsurans* in the stratum corneum. It is a dermatitis, and, according to its intensity, gives rise to the clinical pictures known as *herpes tonsurans maculosquamosus* and *herpes tonsurans vesiculosus.* This is the ordinary superficial "ringworm" of non-hairy parts. A sub-variety is known as *pityriasis rosea* (Gibert).

ii. Eczematous Ringworm (Epidermophytia cruris)

The skin affection, variously known as *eczema marginatum,* **dhobie itch,** and washerman's itch, has been shown to be due to various species of *Epidermophyton.* This fungus varies somewhat from *Trichophyton* in that it never invades the hair or hair follicles. The skin affected is usually that of the crotch, or of the axilla, though the process may be localized between the toes and on the feet where it gives rise to a very chronic form of dyshydrosis. It is prone to attack parts of the body rich in glands, e. g., the genitals, scrotum, crena ani, and axilla. When the process is acute the affected skin is red and swollen; the margin of the area is sharply delimited and may be marked by many small vesicles. The itching is extremely severe. Subsidence and recurrence of the infection are characteristic.

The *diagnosis* can readily be made by cutting off the cap of one of the vesicles with a razor and examining it microscopically in 10 per cent KOH under a cover-slip. The mycelium and spores are usually readily made out. The organism may be grown upon Sabouraud's maltose-agar. Many such cases of years' standing can be readily cured if the parasitic character of the lesion be recognized and parasiticidal remedies applied.

iii. Barber's Itch or Ringworm of the Hairy Scalp and Beard (Trichophytia tonsurans capillatii)

In this form, circles of parasitic invasion appear in the scalp or beard, interfering with the growth of hair, and giving it a "stubbly" appearance, in contrast with the smooth circles devoid of hair in alopecia areata.

The hairs are not killed for they will grow again if the infection be overcome.

iv. Parasitic Sycosis (Trichophytia profunda)

In this disease, the fungus penetrates the follicles and sets up a suppurating folliculitis and perifolliculitis. Abscesses of considerable size may develop. In the region of the beard the disease is sometimes called *sycosis parasitaria,* while on the hairy scalp it is called *kerion celsi.* The disease gives rise to a repugnant sweetish smell.

v. Ringworm of the Nails (Trichophytia unguium)

The fungus here attacks the finger-nails. It is most common in those who have their nails well cared for by manicurists. It rarely occurs among the farming population. The nails lose all their gloss, become rough and nodular, and look splintered; the lateral margins may be elevated. Shavings from the nails, treated with KOH, reveal the fungus, which differentiates the affection from trophic disturbances, syphilis, etc.

Reference

***Morris* (*Sir M.*).** *Parasitic diseases of the skin. In: Syst. Med. (Allbutt & Rolleston). 8°. London, 1911, ix, 117–161.*

(*e*) *Human Microsporon Mycoses*

These include (a) pityriasis versicolor and (b) erythrasma.

i. Pityriasis versicolor

This is due to the fungus *Microsporon furfur,* which has characteristic large gonidia, in grapelike arrangement. None of the other pathogenic fungi of the skin show such large masses of fructification elements (Fig. 89).

A yellowish, or brownish, discoloration of the skin occurs, due to its invasion with this *Microsporon furfur.* It may cover the whole front of the trunk, and is sometimes seen on the arms. Occasionally, only small areas are affected. The disease is accompanied by bran-like desquamation, especially when the skin is neglected. It is rarely seen in parts of the skin not covered by clothing.

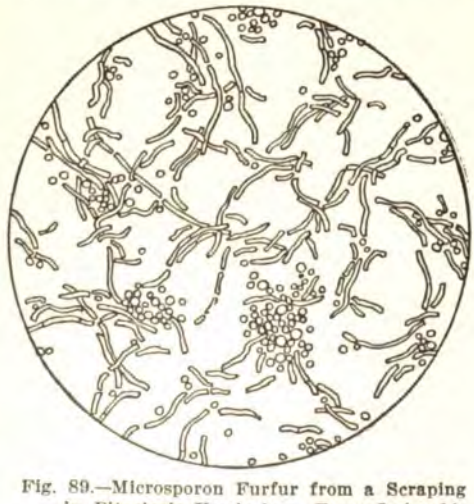

Fig. 89.—Microsporon Furfur from a Scraping in Pityriasis Versicolor. From Jesionek's Article in Riecke's "Lehrbuch," published by G. Fischer, Jena.)

It causes no subjective sensation except, sometimes, slight itching. It occurs most often in persons who sweat freely (flannel underclothing). Tuberculous patients are peculiarly subject to it. It is practically never seen in children nor in the aged.

The diagnosis is easy from the characteristic appearance, and can be confirmed by examining a scraping in KOH under the microscope.

(*f*) *Erythrasama* (*Baerensprung*)

This is an invasion of the skin, by the fungus *Microsporon minutissimum,* which looks like *Microsporon furfur,* except that the threads are much smaller and more delicate. The spores consist of minute granules lying in loose heaps. The sites of predilection in the skin are the scrotum, Scarpa's triangle, the perineum, the folds between the buttocks, the inframammary region, and the axilla.

The infection gives rise to round, yellowish-brown spots, of a reddish tint. These have a pronounced tendency to become confluent, giving rise to areas as large as a silver dollar, or even as large as the palm of the hand.

The **diagnosis** can be confirmed by examining a scraping, microscopically, in NaOH. The disease should not be confused with eczema marginatum (see above) though this name has sometimes been applied to it.

Reference

***v. Baerensprung* (F. W. F.).** *Die Gürtelkrankheit. Annal. d. Charité-Krankenh., Berlin, 1857, Bd. ix, Hft. 2, 40–128.*

2. Mycoses Due to Yeasts and Yeastlike Fungi

The **blastomycetes** or yeast fungi are round or oval, unicellular, nucleated organisms, which propagate by budding. A projection appears on the wall of a cell, and gradually grows larger; the daughter-cell soon assumes the shape of the mother-cell. It then becomes pinched off, or it may remain for a time in connection with it.

Some varieties give rise to endogenous spores (ascospores). Others do not form spores, or have lost the power to do so ("imperfect fungi"). Among the latter, there are varieties that form genuine mycelia and resemble morphologically the eumycetes; they have been called cryptococci, zymonema, monilia, oidia, dematia, etc. In other words, the term blastomycetes is an omnium gatherum for fungi of wholly different origin, propagation by budding alone being common to them all. Botanically, the name and the group are very unsatisfactory, so that the botanists urge that we do away entirely with the term *Blastomyces,* and replace it

by terms technically more satisfactory. Thus, Vuillemin, a distinguished French investigator, instead of using the term "blastomycoses" for the diseases produced by these fungi, suggests that we call the diseases produced by the spore-formers *exascoses,* and the diseases produced by budding fungi, like oidia, *oidiomycoses.* If the fungus turns out to be a variety of endomyces, the disease it causes is known as an *endomycosis.* As Plaut points out, however, such a classification, while more correct, is difficult for the clinician to apply; thus, for example, the same clinical affection (thrush), when it is produced by yeasts that form ascospores, would have to be designated an endomycosis, or saccharomycosis, but if produced by yeasts not forming such spores would be called a parasaccharomycosis or moniliomycosis. If in place of these terms we use the single word *thrush-mycosis,* every physician knows immediately what we mean.

It is therefore convenient for the present to retain the term *blastomycosis,* meaning by it a disease caused by budding fungi, which as a rule have no mycelium, and possess the capacity of forming endogenous spores. Mycoses due to similar fungi that produce mycelium may be called *oidiomycosis,* if they morphologically resemble the well-known oidium lactis. Should the fungi belong to the thrush-fungus group, we can separate these out as a special group—the *thrush-mycoses,* notwithstanding the fact that this group may include different species belonging either to endomyces or to monilia. When the fungi are not closely related to the budding fungi, but are characteristic in their morphology, we give them names based upon their form (e. g., sporotrichosis, hemisporosis, etc.).

It may be convenient to have the French classification of this group of diseases. That used by de Beurmann and Gougerot is as follows:

EXASCOSES

(A) *Saccharomycoses and Atelosaccharomycoses.*—These give rise to the ordinary blastomycoses. In this group belong monospora, saccharomyces, cryptococcus, and endomyces. These species, as a rule, do not give rise to mycelium.

(B) *Parasaccharomycoses.*—This group of diseases stands between those in A and in C. The fungi form mycelia.

(C) *Zymonematoses ("Yeast Threads").*—This group includes the oidiomycoses (e. g., Gilchrist's disease). The fungi form mycelia in growths on culture media, and multiplication by budding can be made out in the pus and in the tissues. No endosporulation is seen.

(D) *Parendomycoses.*—The fungi causing these diseases stand midway between C and E in their morphological behavior. Here belong the fungi causing remarkable diseases in horses (Tokishige's disease, and the epizoötic lymphangitis of Rivolta and Micellone). The fungus of the

coccidioidal granuloma of the San Joaquin valley probably belongs here; in the pus, endosporulation occurs but no budding forms are seen.

(E) *Endomycoses.*—These include the diseases due to thrush fungi of the endomyces type, whereas the thrush fungi of the monilia type would, by the French, be excluded from the exascoses.

(*a*) *The Blastomycoses and Coccidioidal Granuloma*

These affections of human beings and animals are due to yeast-like organisms (see above).

i. Blastomycetic Dermatitis and Systemic Blastomycosis

Definition and Etiology.—Blastomycosis is a disease due to a budding fungus—*Cryptococcus gilchristii.* Obtained from the lesions in which it occurs, it appears as a spherical cell surrounded by a refractive membrane, the diameter of the yeast varying between ten and sixteen microns. In the pus one often sees a pair of cells, one larger and one smaller, the smaller one having been budded off from the larger. The fungi are often enclosed within the bodies of phagocytes (giant cells). They are easily demonstrable in fresh pus or fresh tissue by treatment with a solution of caustic soda. No endosporulation is seen in the fungus in tissues or in pus. The fungus grows well on acid media, but the initial growth is slow, requiring from ten days to two weeks for definite development, though after prolonged cultivation it may grow out in a few days. The optimal temperature for growth is 20° C. Rabbits and guinea-pigs are susceptible to infection with this fungus, but less so than for the fungus of coccidioidal granuloma (see below).

Fig. 90.—Sediment from Tissue Disintegrated in 50 per cent Alcohol, Showing Blastomyces in Various Stages of Budding. (After F. H. Montgomery and O. S. Ormsby, Arch. Int. Med.)

Forms of the Disease.—Two main forms have been distinguished: (1) blastomycetic dermatitis and (2) systemic blastomycosis.

Blastomycosis of the skin is usually primary. It appears as an acne-like process, later giving rise to ulcers and cauliflowerlike excrescences. It often begins about the nose or the eye, or the side of the neck. Metastases in the internal organs (lungs, brain, bone) are not uncommon.

In systemic blastomycosis the infection probably occurs by inhalation, as the respiratory tract seems to be first infected, and the early symptoms are referable to the lungs in which signs of a bronchopneumonia develop. Later the infection becomes generalized, and small or large abscesses occur

in the skin, subcutaneous tissue, lymph glands, muscles, bones, nervous tissues and viscera. The abscesses may range in size from minute areas to large cavities containing a quart of pus.

Symptoms.—In blastomycetic dermatitis pustules and local ulcerations or subcutaneous abscesses appear in the skin. The lesions are multiple and may occur successively or in crops. An ulcer may be primary, or it may develop at the site of a ruptured abscess. The chronic ulcers

Fig. 91.—Skin Lesions in a Case of Blastomycosis. (After B. W. Fontaine, M. Haase and R. H. Mitchell, Arch. Int. Med.)

often present a fungoid appearance, the surface being nodular or papillomatous. Blastomycetes can be found in the pus by mounting a little of it fresh or by mixing some of it with a 20 per cent solution of NaOH.

In systemic blastomycosis the patients usually report that their illness began with a cold or some acute respiratory infection, often with a chill, pain in the chest, fever, shortness of breath, cough and expectoration. Later on, characteristic subcutaneous abscesses appear. In some instances, no acute stage is reported, but small subcutaneous abscesses or local ulcerations of the skin first attract the patient's attention. Once the disease is well established, the symptoms of a chronic infection become evident. The patients emaciate, grow weak, and complain of pain in the affected part; the pulse is accelerated, there is irregular fever, and occasionally there are chills and sweats. In most cases signs of pulmonary involvement are demonstrable. Often the blastomycetes can be demon-

strated in the sputum; occasionally they can be isolated in blood cultures or in cultures made from the urinary sediment. Pains in the bones and joints may herald a localization in these structures. Paralyses may occur owing to the presence of lesions in the spinal cord or brain. A secondary anemia develops, usually with a marked leukocytosis, sometimes

Fig. 92.—Characteristic Lesions of Cutaneous Blastomycosis. (After F. H. Montgomery and O. S. Ormsby, Arch. Int. Med.)

as high as 30,000 w. b. c. per c.mm. In Stober's series the average leukocytosis was 16,800. When the bones are involved, there may be an irritation myelocytosis.

In *Gilchrist's form* the parasite appears in the tissue only as a yeast, though, in cultures, it forms threads and conidia, like oidium. With Dr. H. C. Buswell, of Buffalo, I saw a remarkable instance of infection with this organism. There were multiple, small, subcutaneous abscesses present in the pus from which Dr. Clough isolated the fungus. Later the

patient developed a nodule on his tongue, suggestive of carcinoma; a piece was excised for diagnosis, and, on examination, Dr. Welch found that it was a granuloma due to the same fungus!

Diagnosis.—When multiple subcutaneous nodules or abscesses appear in a patient, some of the pus, or a piece of the tissue, should always be examined in a solution of NaOH for the fungus. In obscure pulmonary infections and in atypical lesions of bones and joints, systemic blastomycosis should be kept in mind as a possibility. The diagnosis is rendered certain by the demonstration of the blastomycetes in the pus, sputum, urine, or blood, or in histological sections of infected tissues excised for diagnostic purposes. With such a simple method at our command there is now no excuse for not recognizing the disease when it exists. Fresh material is far better than stained preparations, since in the latter the fungi are easily overlooked.

Differential Diagnosis.—Blastomycetic dermatitis and systemic blastomycosis must be differentiated: (1) from *coccidioidal granuloma* (closer resemblance to tuberculosis; involvement of lymph nodes more common; cutaneous lesions more ulcerative; disease fatal and not amenable to treatment with KI; fungus shows endosporulation and not budding in pus and tissues; initial growth of fungus in cultures more rapid; fungus more pathogenic for rabbits and guinea-pigs); (2) from *tuberculosis* (cavity formation and hemoptysis more common; tubercle bacilli in sputum; cutaneous lesions uncommon, except when lupus is present; Calmette reaction positive); (3) from *syphilis* (Wassermann reaction; absence of blastomycetes); (4) from *sporotrichosis* (q. v.); (5) from *epithelioma* (slower growth; greater induration; absence of fungus; histology).

ii. Coccidioidal Granuloma

(*California disease; San Joaquin Valley disease; Mycoderma immite*)

Definition and Etiology.—A disease due to a peculiar fungus that has received various names *Oïdium protozonide; Oïdium coccidioide; Coccidioides pyogenes; Posadasia esseriforme,* etc.

The fungus was discovered by Wernicke, in 1892, in a Brazilian soldier affected with a peculiar cutaneous lesion. A careful study of the condition was made by Posadas, who inoculated animals with fragments of the diseased tissue. In the lesion, the fungus occurs in the form of spherical cells, varying from 3 to 80 microns in diameter, and surrounded by a thick refractive membrane. Spores are formed inside the cells (endosporulation). In cultures, though not in tissues, the fungus grows out into mycelial filaments, just as does the blastomycetic fungus. The initial growth is more rapid than for blastomycetes, some growth being noted at the end of twenty-four hours. The optimal temperature for growth is 37° C. Animal inoculation yields well-defined endosporulating organisms. Budding forms do not appear. Rabbits and guinea-pigs are susceptible to infection, as are also monkeys and mice. Like blastomyces this coccidioidal fungus can give rise either

to an inflammation and ulceration of the skin (coccidioidal dermatitis), or to a general systemic involvement with lesions in the lungs, kidneys, liver, spleen, suprarenal capsule, bones and jonts (systemic coccidioidal granuloma).

Symptoms.—As met with in California, the disease is nearly always, and often rapidly, fatal. The symptoms closely resemble those of tuberculosis. The infective agent shows a greater predilection for the lymphatic system than in blastomycosis, and the cutaneous lesions of coccidioidal granuloma tend to be more ulcerative. The iodides, so efficacious in blastomycosis, seem to be without effect in coccidioidal granuloma. The disease occurs most often in males, and in foreigners living in this country. Occasionally, a female is attacked.

Diagnosis.—This depends upon the demonstration of the peculiar fungus in the lesiou. Fresh specimens treated with from 4 per cent to 20 per cent NaOH should be examined. The absence of budding and the existence of endosporulation distinguish this fungus from the blastomyces (see above).

The frequent occurrence of yeast-like fungi in carcinoma, and in other tumors, has been the subject of especial study by Sanfelice; for a time, it was thought that the fungi were etiologically related to the neoplasms, but this view is no longer held.

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(*b*) *Diseases Due to Thrush Fungi*

i. Thrush

This disease is described under Stomatitis in the section on Diseases of the Digestive Apparatus.

The Thrush Fungi.—We have come to learn that many different, though probably related, fungi may cause what is known, clinically, as thrush. Part of these fungi are "imperfect fungi," and cannot be classified, otherwise, botanically. Some forms, however, belong definitely among the *Ascomycetes.* The most common form met with in the thrush of children is a thread-fungus, which not only produces mycelia, but also multiplies by budding. It grows easily on all nutrient media, though preferably in acid media containing sugar; it ferments sugar and will grow either aërobically or anaërobically; in the presence of oxygen, the budding forms are prominent; on exclusion of oxygen, mycelia with conidia develop. In addition to the forms of propagation just mentioned, one sometimes sees chlamydospore formation, and ascospores.

The variety that forms true ascospores in the pseudomembrane is called *Endomyces albicans.* Still oftener, the disease is due to *Monilia candida Bonorden;* thrush is sometimes due, also, to a pure budding form.

Characteristics of Endomyces albicans.—In cultures, mycelia develop, which show oidium-formation at the ends; spherical chlamydospores may be seen singly, or in pairs, at the tips of the mycelia. Endoconidia are formed in the mycelia, and also outside them, on the lateral

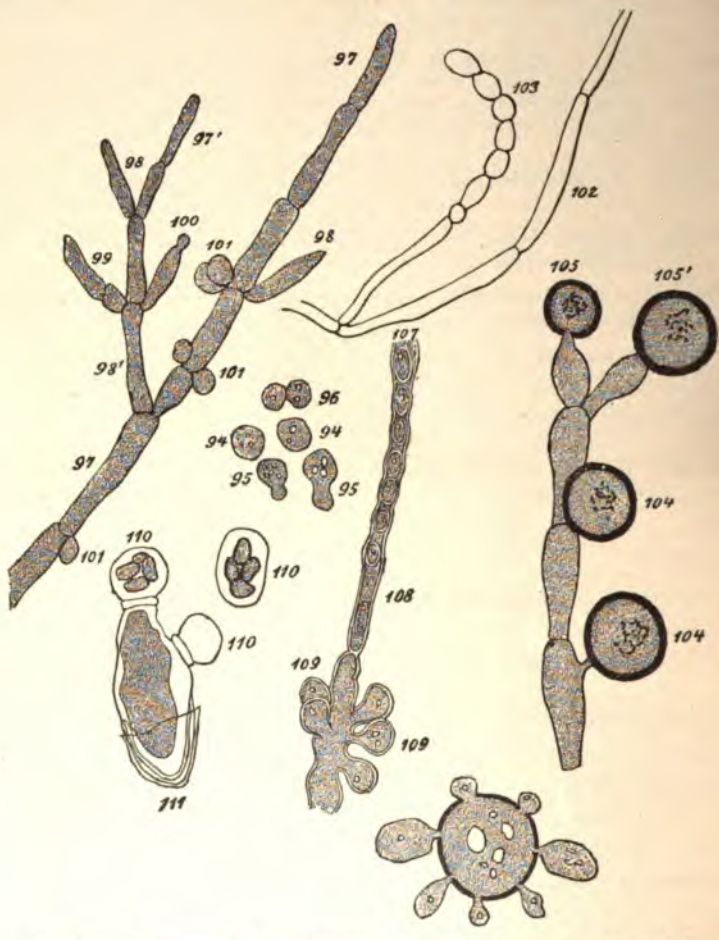

Fig. 93.—The Thrush Fungus—94-96=Spores; 97-102=Mycelium; 104-105=Chlamydospores; 110-111=Ascospores. (After Vuillemin, in H. C. Plaut's "Spez. Path. u. Ther. inn. Krankh.," published by Urban & Schwarzenberg, Berlin.)

surface of the mycelium threads. The asci may be located either at the tip of a thread, or in its course; they are elliptical, or oval, and contain 4 spores in a delicate membrane, which quickly disappears.

Characteristics of Monilia candida Bonorden.—Two varieties may be distinguished, a large-spored variety, the *Oidium albicans* of Robin, and a small-spored variety, the *Saccharomyces non-liquefaciens* of Fischer.

The large-spored variety is the commoner. It differs from the Endomyces albicans chiefly in the fact that no asci are formed. In cultures, it multiplies by budding, like the yeasts, but it may grow like monilia with mycelium formation. The chains of conidia from the sides of the threads and from the ends of the mycelia, are prominent features. Mycelium formation is favored by anaërobic conditions, by an alkaline medium, and by scarcity of carbohydrate in the medium; the budding process is favored by a medium rich in sugar, by an acid medium, and by aërobic conditions.

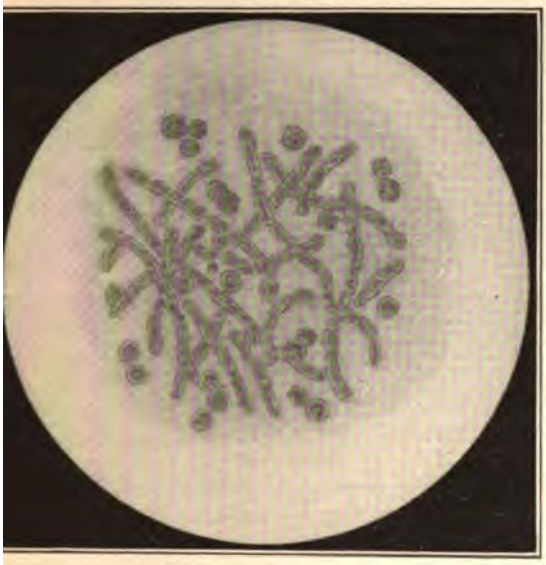

Fig. 94.—Oidium albicans. (After N. D. Jagic and H. K. Barrenscheen, "Atlas u. Grund. d. Klin. d Mikroscopie," published by M. Perles, Wien.)

On gelatin, or on agar, the thrush fungus grows superficially as a snow-white hemispherical layer; in deep colonies, fine feathery threads grow out from the periphery.

For a full account of these different varieties of thrush fungi, see Plaut's article in Kolle and Wassermann, V, 50.

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3. Mycoses Due to Sporotrichum and Related Fungi

(*a*) *Sporotrichoses* (*Schenck's Disease*)

Sporotrichum.—This is a fungus belonging to the *Hyphomycetes;* family, *Mucedinaceæ;* sub-group, *Botrytideæ,* and is closely related, botanically, to the fungi that cause favus, ring-worm and pityriasis. No less than 120 varieties of *Sporotrichum* are already known. The fungus grows in nature on rotten wood, decaying plants, old walls, etc. The hyphae are branched. Oval or spherical conidia arise at the ends of short sterigmata.

Historical.—This disease was discovered in Baltimore. A patient, suffering from a peculiar ulceration of the hand, with induration of the forearm, applied for treatment in the surgical out-patient department at the Johns Hopkins Hospital, in November, 1896. It was made the object of especial study by Dr. Schenck, now the gynecologist of Detroit, who isolated, in cultures, a branching fungus, giving rise to mycelium and spores; it was submitted to Dr. Ervin F. Smith of Washington, who identified it and gave it the name *Sporotrichum schenckii.* The case was reported in the Johns Hopkins Hospital Bulletin, in 1898. Two years later, a careful study of the same fungus from a second case, was reported by Hektoen and Perkins, in the Journal of Experimental Medicine, under the title "Refractory Subcutaneous Abscesses Caused by *Sporothrix schenckii.*" In both cases, a nodular lymphangitis of the arm had followed an infection of the finger. Since this discovery, the disease has been found in various parts of the world; it seems to be especially prevalent in France.

In 1903, de Beurmann, of Paris, reported a number of cases of sporotrichosis. While the credit of the discovery of the disease undoubtedly belongs to American observers, great credit is also due to the French physicians, for having shown, (1) the frequency of the disease, (2) its resemblance in many cases to tuberculosis and to syphilis, and (3) the importance of separating it from these diseases, since it can be speedily and completely cured by medical measures, namely, by large doses of potassium iodid. Many individuals, falsely held to be luetic or tuberculous, have been freed from their disease, in a remarkably short time, through the making of a correct diagnosis of sporotrichosis and the institution of an appropriate therapy.

Properties of the Fungus.—The sporotrichum, when examined in the tissues affected, may lie either outside of cells, or inclosed within macrophages. It is a rod-shaped, oblong, somewhat granular body, 3-5 μ long and 2-3 μ broad. It is surrounded by a pale membrane, which remains unstained in ordinary dyes, while the protoplasm is basophilic. It is very difficult to find the fungus in the disease focus, so difficult that there is but little use in looking for it as a diagnostic measure. It can, however, be easily grown from the lesions, on culture media. In cultures, it is a genuine mycelial fungus, divided by septa; it shows round or oval ectospores, which, pedicellate or unpedicellate, may form large groups, or may be seen singly, surrounded by threads of mycelium. The

microscopic examination of the culture alone will not suffice for diagnosis; one has to rely upon the macroscopic appearance. The growth begins as

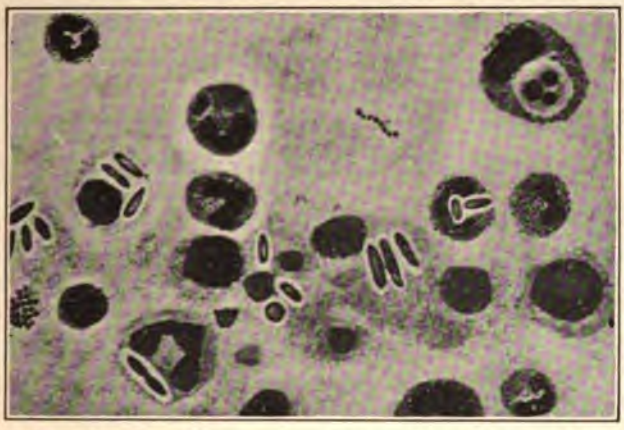

Fig. 95.—Sporotrichosis beurmanni, Smear from Lesion. Parasites are of Unequal Size, 2-5 μ Long and 2-3 μ Broad. (After H. C. Plaut, "Spez. Path. u. Ther. inn. Krankh.," published by Urban & Schwarzenberg, Berlin.)

a fine mycelial star, colorless, or waxy-looking. As the growth proceeds it forms a folded membrane, resembling the appearance of a walnut, or the gyri of a cerebral hemisphere. Gradually the culture becomes dis-

Fig. 96.—Sporotrichosis. (A) Young Thread-forming and Spore-bearing Hyphae. (B) Older Hyphae with Numerous Spores. (After Gougerot, in H. C. Plaut's "Spez. Path. u. Ther. inn. Krankh.," published by Urban & Schwarzenberg, Berlin.)

tinctly yellowish-brown in color. Later on, the center presents a blackish, rusty appearance, due to spore formation; at this time, the appearance of the culture is very characteristic, and suffices for diagnosis.

Thus far, five distinct pathogenic varieties of sporotrichum have been described, depending upon the optimal temperature for growth, polymorphism, pathogenicity, toxin formation and cultural properties. The details of the differentiation of these different varieties will be found in the excellent article by Gougerot (Die Sporotrichose, in Kolle and Wassermann, 2te Aufl., V, 236).

Symptoms of Sporotrichosis.—Any tissue of the body may be affected, though the skin is most often involved. Nodules like gummata appear, but show a marked tendency to soften, and to break down. These nodules may be single or multiple. Sometimes the ulcers resemble tuberculous ulcers, or they may suggest ecthyma. Large subcutaneous abscesses, difficult to heal, were observed in the cases described by the discoverer, Schenck and by Hektoen and Perkins. In some cases, papillomalike, warty efflorescences appear. The condition is often diagnosed "warty tuberculosis" of the skin, or as "gumma." Most of these cases are seen first by the dermatologist. The internist is more likely to see the cases of sporotrichous sore throat, or sporotrichous affections of the bones, joints, and synovial sheaths. In some cases, the disease runs the course of a bronchopneumonia, in others, of a pyelonephritis.

Fig. 97. — Sporotrichotic Gumma; Multiple Fistulae, Separated by Bridges of Non-ulcerated Skin. (After de Beurmann and Gougerot, in H. C. Plaut's "Spec. Path. u. Ther. inn. Krankh.," published by Urban & Schwarzenberg, Berlin.)

Some of the most puzzling cases are first seen by the surgeon, and are taken to be gummata, or tuberculosis of the bones or of the joints. Sporotrichosis of the larynx, and of the eye, are also known.

The following characteristics are emphasized by Gougerot: (1) numerous lesions, without marked impairment of the general condition; (2) beginning in the form of painless nodules, with partial softening, and gradual abscess formation; (3) jagged margins to the ulcerations, violet color of the margins of abscesses, pigmentation and undermining of the margins of ulcers; (4) contrast between the slight extent of the ulceration and the distribution of the softening; (5) presence of several openings, or of two ulcers lying opposite one another for one infiltrated area, and union of the ulcerated areas by a narrow bridge of violet colored skin; (6) mucoid or citron-yellow fluid; (7) ease of auto-inoculations; (8) cold, indolent swellings; (9) cicatrization, with persistence of the abscess beneath the skin; (10) flat, narrow, or broad, soft scars, with jagged and pigmented edges. Lymph glands not enlarged.

Prognosis.—If recognized in time, and a vigorous iodin therapy instituted, the prognosis is favorable.

(*b*) *Other Mycoses Resembling Schenck's Sporotrichosis*

Clinical phenomena, exactly like typical sporotrichosis, can be due to other fungi. Of these, several varieties are already known (*hemisporosis, acremoniosis, bothrytimycosis, cladiosis,* etc.).

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4. Mycoses Due to the Different Varieties of Streptothrix

(*The Streptotrichoses, Cladioses, Nocardoses, etc.*)

Streptothrix.—This term was originally used, by Corda, for a microorganism different from that to which the name is now applied. What is now known as streptothrix was described first by F. Cohn as *Streptothrix foersteri,* and was the name given to a fungus first found in the lachrymal duct. On account of the previous use of the name by Corda, French botanists prefer to use some name other than streptothrix for the organism we are now considering. Vuillemin, for example, calls it *microsiphomyces,* and de Toni and Trevisan suggest that the whole class be included under the name *Nocardia,* in honor of the French veterinarian Nocard, who investigated these fungi in animals. Accordingly, in the French literature the diseases due to streptothrix are spoken of as *nocardoses.*

It may be convenient to have the classification followed by the French and schools before us:

	French Classification		*German and American Classification*
1. Group. Actinomyces.	Nocardoses, Granules with clublikes wellings.	Actinomyces Harz.	Typical actinomycosis.
		Actinomyces bovis.	
		Actinomyces Israeli, Ravaut et Piney, Thibergi.	
	Nocardoses, with white or yellowish granules, without club formation.	Actinomyces Moorhof, Poncet-Dor, Hesse, Garten, Doepke.	Atypical actinomycosis.
2. Group. Mycetoma.	Mycetoma blanc. Vincent	Nocardia Maduræ.	Madura foot.
	" actinomycosique	" bovis.	
	" "	" Eppinger.	
	" "	" Carougeau.	
3. Group. Nocardia Eppinger.	Nocardia asteroides Eppinger.		Pseudoactinomycoses. Streptotrichomycoses.
	" " "	Var. Rivieri	
	" " "	Var. Japonica	
	" " "	Var. Ferrei	
4. Group.	Nocardosis of Carougeau.		Discomyces Carougeaui.
5. Group.	Erysipeloid of Rosenbach.		Rotlauf bacilli.

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(*a*) *Typical Actinomycosis in Human Beings*

Streptothrix actinomyces. — The *ray-fungus,* or *Streptothrix actinomyces,* occurs as a spore-bearing mycelium. In the human body, peculiar whitish-yellow granules, or "glands," are thrown off. They may be visible to the naked eye in sputum, so-called "sulphur granules"; on microscopic examination, flasklike enlargements of the threads may be seen at the margin.

The fungus is not easy to grow in culture-media; out of about 60 tubes inoculated, one is lucky to get 4 or 5 cultures. Some varieties grow aërobically, others anaërobically. The best medium is coagulated blood serum to which glycerin has been added; glucose-bouillon (1 per cent), and potato, are also satisfactory media.

The fungus is common in cattle (Bollinger, 1877), horses, goats, pigs, and sheep. It is the cause of the "lumpy jaw" of cattle. In order that human beings may be infected, some irritating foreign body (barley grain, splinter) must

accompany the germ. The fungus was found in a disease of the human spine by Langenbeck in 1845, and the mycosis in human beings was very exactly described by J. Israel in 1878. A good review of the bibliography up to 1911 will be found in the article by M. Schlegel. The portal of entry in human beings is usually the mucous membrane of the mouth, the tongue, or the tonsils; sometimes the primary focus is in a carious tooth.

Symptoms.—These are variable, according to the portal of entry.

In ORAL ACTINOMYCOSIS, swelling of the submaxillary and of the submental regions or of the margin of the gum appear; hard at first, these later undergo softening, with pustule formation. Infection through carious teeth causes subperiosteal growth, with swelling and tumor formation.

The subcutaneous tissue is sometimes involved (DERM-ACTINOMYCOSIS). Actinomycosis of the skin involves most often that of the neck and head, leading to the formation of nodular masses that soften, ulcerate, and discharge characteristic pus. The course is extremely chronic.

In PULMONARY ACTINOMYCOSIS, the infection may arise through aspiration of the fungus in dust, or, secondarily, by extension from the neck. The yellow actinomyces particles are coughed up, and appear in the sputum. The inflammation may extend to the pleura. The symptoms include irregular fever, cough, and expectoration, the clinical picture closely resembling that of pulmonary tuberculosis. The physical signs may be those of bronchitis, of bronchopneumonia, or of pulmonary excavation.

INTESTINAL ACTINOMYCOSIS also occurs, especially in parts in which there is often fecal stasis (cecum, vermiform appendix, colonic flexures, rectum). It gives rise sometimes to diarrhea, sometimes to chronic peritonitis, often to symptoms resembling chronic appendicitis. A GENERALIZED ACTINOMYCOSIS, or septicemic form has also been described.

Diagnosis of Actinomycosis.—The disease often goes long unrecognized, until the characteristic "sulphur" granules are found. Still, in the well developed stage, the condition is very characteristic; the chronic inflammation of low grade, the insidious course, the slight discomfort to the patient at the beginning, the combination of tough connective tissue masses with softened areas, the fistula-formation giving rise to a coarse-sieve-like appearance to the skin, are striking features.

Actinomycosis must be distinguished in the skin: (1) from *lupus,* (2) from *gumma,* and (3) from *tuberculosis;* in the tongue, (4) from *carcinoma,* and (5) from *blastomyces;* in the lung, (6) from *tuberculosis,* (7) from *syphilis,* and (8) *from neoplasm;* in the intestine, (9) from *appendicitis,* and (10) from *periproctitis,* etc.

It is well to follow the advice of Poncet and Thevenot, who suggest that whenever one thinks of tuberculosis, cancer, or syphilis, he should think of the possibility of actinomycosis.

If typical, club-shaped swellings are not present, one can try by culture to determine whether he is dealing with (1) a true or typical actinomycosis, (2) an atypical actinomycosis, or (3) a pseudo-actinomycosis (actinobacillosis, or streptotrichomycosis).

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(*b*) *Mycetoma* (*Madura Foot*)

Definition.—A chronic infectious process, characterized by the formation of multiple granulomatous nodules, beginning usually on the plantar surface of the foot. The tumors soften, and sinuses are formed that can often be traced between the bones of the enormously enlarged and greatly deformed foot. Characteristic streptothrix forms may be found in the mucopurulent discharge. The disease is sometimes mistaken for syphilis or for sarcoma. Occasionally, parts of the body other than the foot are invaded; thus involvements of the abdomen, of the head, and of the hand are known. The disease was first described, in 1712, by Kämpfer.

The disease is common in India, but occurs also in Africa, in South America, and in the Philippines; it has been observed also in Italy, in Roumania, and in Greece. In India, Carter recognized the similarity to actinomycosis. Boyce and Surveyor (1894) pointed to the clinical differences between the two diseases. Vincent (1894) was probably the first to isolate a fungus in pure culture from Madura foot, but now no less than 11 different fungi have been separated from different forms of the disease; 6 of these are associated with "yellow granules," 5 of them with "black granules."

The Mycetoma Fungi.—The fungi occur in the pus, and in the tissues, either as yellow granules, or, less commonly, as black or melanoid granules, according to the variety. Each granule consists of masses of a hyaline, brownish, brittle substance, which has a matrix, in which is imbedded the mycelium. The fungi from yellow granules grow like *streptothrix*, or *Indiella;* those from black granules do not, but seem to be forms of *aspergillus*, and of *Madurella*. One of the fungi, *Streptothrix freeri*, has been grown in Manila by Musgrave and Clegg; successful cultures have also been made from Madura foot by J. H. Wright of Boston.

Mycetoma differs from actinomyces in several important respects: (1) it attacks, by preference, the foot, which is hardly ever attacked by actino-

myces; (2) a generalization of the fungus does not occur; (3) the course is more chronic than in actinomycosis, extending over decades; (4) spontaneous cure does not occur; and (5) the iodin treatment, so beneficial in actinomycosis, is not efficacious in mycetoma.

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(*c*) *The Pseudo-Actinomycoses or Streptotrichomycoses*

The lungs, the brain, the skin, the digestive tract, and the eye may be invaded by streptothrix forms. According to Foulerton, of 78 cases collected from the literature 65.4 per cent were in men, 34.6 per cent in women; 51.2 per cent of the cases were primary in the mouth and neck, 25.6 per cent in the appendix, 18.1 per cent in the lungs, and 5.1 per cent in the eye, kidney or bladder.

Lungs.—The streptotrichomycoses of the lungs closely resemble pulmonary tuberculosis clinically and pathologically. Thus S. Flexner has described the process as *Pseudotuberculosis hominis streptotricha.* The streptothrix can be found sometimes in the sputum; it can be distinguished from the tubercle bacillus by the fact that (1) it is longer, (2) the individual members of the chains are of equal length, while the granules of tubercle bacilli are irregularly arrayed, and (3) the streptothrix is somewhat less acid-fast.

The streptothrix shows branching forms. The varieties of pathogenic streptotriches and their group relationships to other acid-fast organisms have been especially well studied in this country by Edith Claypole.

Digestive Tract.—Stomatitis, tonsillar abscess, pyorrhea, noma, esophagitis, enteritis, and appendicitis are among the conditions in which streptothrix may be found as a causative agent.

Skin.—Cutaneous infections are fairly common, and may give rise to metastatic infection of the organs. In one case, reported by Fränkel and Schottmüller (1912), in which a laboratory worker became infected after a rat-bite, a septic

process developed and ended fatally; large colonies of streptothrix grew in plate-cultures made from the blood during life.

Brain.—Metastatic abscess of the brain may thus arise, and simulate tuberculosis. In the well-known case, reported by Eppinger (1890), a chronic abscess of the brain broke into the ventricle, and caused purulent meningitis. At autopsy, foci were found in the lungs, supraclavicular lymph glands, and in the brain; all of them contained streptothrix-threads, reported by Eppinger as a pathogenic cladothrix—*Nocardia asteroides*. The organism was pathogenic for rabbits and guinea-pigs but not for mice. In the experimental animals, lesions like those of miliary tuberculosis were produced (pseudotuberculosis). Similar streptothricoses have been studied by Sabrazès and Riosère and by Ferré and Faguet.

Eye.—The first streptothrix (Streptothrix försteri) was obtained from the lachrymal duct. Keratitis and conjunctivitis sometimes occur, due to the same fungus.

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(*d*) *Discomyces Mycoses*

In the tropics, Jeanselme has described a disease resembling somewhat Madura foot but not identical with it. Nodules of the size of a hazel-nut or larger develop in the subcutaneous tissue about the large joints. It is painless, disturbs the patient but little, but is a protracted disease. The lesions are exceedingly like tubercles, containing giant-cells and undergoing caseation in the center. The disease is due to a discomyces (Gougerot, 1909; Fontoynont and Carougeau, 1910); it is sometimes called the nocardosis of Carougeau.

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II. DISEASES DUE TO ANIMAL MICROÖRGANISMS (PROTOZOA)

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A. Diseases Due to Pathogenic Rhizopoda

Under this heading will be described the diseases due to pathogenic amebae. The rhizopoda are characterized by the fact that they have pseudopodia but no flagella.

Amebae.—The amebae are cells usually somewhat larger than white blood corpuscles, with strongly refractive protoplasm. On a warm stage, they show lively ameboid movements. Often a clear hyaline *ectoplasm* can be distinguished from a granular *endoplasm*. The protoplasm contains vacuoles, and sometimes bacteria and red blood corpuscles. The nucleus is vesicular. *Vegetative forms* are distinguished from the *encysted forms*.

Amebae are difficult to cultivate, but cultures have been made in symbiosis with bacteria. Amebae were first seen in dysenteric stools by Loesch (1875), who named the organism *Ameba coli*. Kartulis first produced experimental infection in cats. Kruse and Pasquale ruled out bacteria as the cause of the disease. Councilman and Lafleur showed that besides the pathogenic *Ameba dysenteriæ* a harmless ameba may be present in the stools. This harmless **Entameba coli** may occur in normal persons, but it is seen more often in chronic diarrhea. The pathogenic **Entameba histolytica** (Schaudinn, 1903) is the cause of amebic dysentery and of tropical liver abscess. The disease can be produced in cats by experimental inoculation of the rectal mucous membrane. Sellards and Baetjer (1914) have kept the disease going for more than 10 passages through cats by injection into the large intestine after laparotomy. In the stools, the amebae are best looked for in flecks of mucus, or blood.

Viereck (1907) endeavored to distinguish an additional species, *Entameba tetragena* (nucleus visible during life, always spherical, and possessing a definite limiting membrane; 4 nuclei in the mature cyst); this view was supported by Hartmann, but more recent studies (Craig; Sellards and Baetjer) indicate that E. histolytica (of East Asia and Egypt) and E. tetragena (of Africa and S. America) may be one and the same species. In both forms, the formation of chromidia and of cysts has been carefully followed.

In certain cases of mild dysentery, an actively motile flagellate is sometimes present which is neither cercomonas nor *Entameba histolytica*. An especial species has been described by Craig as *Parameba hominis* and afterwards renamed by others *Craigia hominis*. Marlowe has described about thirty cases of craigiasis in Honduras.

1. Human Amebiasis

Under this heading, we include Amebic Dysentery, Amebic Abscess of the Liver, and Amebic Pyorrhea.

(*a*) *Amebic Dysentery*

Occurrence.—This disease, very common in the tropics, is widespread, also, in the Southern United States. We meet with it frequently in the clinic in Baltimore.

Symptoms.—The symptoms are usually those of a *chronic dysentery*

(alternating periods of constipation and diarrhea with tenesmus; mucus and blood in the stools; abdominal pain and frequently symptoms of disturbed digestion). During the exacerbations of diarrhea, there is often slight elevation of the temperature, tachycardia, colic, lassitude, headache, prostration, dry skin, and scanty urine and saliva. The general state of nutrition is good, at first, in contrast with that seen in *acute* and *subacute types* of the disease. Rarely a perforative peritonitis or a hemorrhage from the bowel occurs.

The disease is frequently overlooked, simply from failure to examine the feces, microscopically, in cases of chronic diarrhea. The mucus accumulated in the "eye" of a rectal tube is particularly suitable for examination (warm stage).

Some cases of amebiasis have an *acute onset* with (1) abdominal pain, often intense, (2) tenesmus constant and severe, (3) a marked intestinal flux with very frequent evacuations of blood and mucus, and (4) rarely, the passage of large amounts of blood, or sloughs from ulcers. There may be (5) slight pyrexia. There is usually (6) eosinophilia. The prolonged diarrhea may lead to (7) extreme emaciation. Death may occur in from one week to three months from inanition and exhaustion. Some of the cases of this type pass over into the chronic form of the disease.

Diagnosis.—This is easy, if one *thinks* of the possibility of the diarrhea being due to *amebiasis,* and examines the stool microscopically for amebae. A proctoscopic examination may reveal the characteristic undermined ulcers in the rectum. The therapeutic test confirms the diagnosis, for the amebae quickly disappear under the use of salol coated pills containing *ipecac* (70 grains per day), or under hypodermic injection of *emetin hydrochlorid* (Rogers). (For a further description of amebae in feces, see Part VIII.)

(*b*) *Amebic Abscess of the Liver*

This is common in hot countries (**tropical liver abscess**). It is really not an abscess, but a widespread necrosis, with softening, often without marked leukocytosis. It is one of the most frequent complications of amebic dysentery, occurring in about 20 per cent of the cases at the Johns Hopkins Hospital.

The abscess may be single, or multiple. It most often involves the right lobe of the liver, especially at its convexity (x-ray examination; increase in dullness on percussion). The disease may be entirely latent; more often it is accompanied by irregular fever, sweats, chills, local pains, and enlargement of the liver. Leukocytosis, 15,000-16,000, with eosinophilia, is common. Amebic abscesses of the liver sometimes break through into the lung, and the diagnosis is first made by finding amebae in the anchovy-sauce sputum. (See also Hepatic Abscess in Part VIII.)

(c) *Amebic Pyorrhea*

This disease, known also as Riggs' disease, and associated with the presence of *Entameba buccalis,* will be described in Part VIII under Pyorrhea alveolaris.

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B. Diseases Due to Pathogenic Mastigophora, or Flagellata

Several relatively unimportant flagellates are occasionally met with as human parasites: (1) *Trichomonas vaginalis;* (2) *Trichomonas intestinalis;* (3) *Lamblia intestinalis* (*Megastoma entericum*); (4) *Cercomonas hominis*).

Certain very important human diseases are, however, due to the following pathogenic flagellates; (5) Pathogenic *Trypanosomidæ* (*Trypanosoma gambiense; Trypanosoma rhodesiense; Schizotrypanum cruzi*); (6) pathogenic *Piroplasmidæ* (*Leishmania donovani; Leichmania infantum; Leishmania tropica*); (7) pathogenic *Plasmodidæ* (*Malaria*), 3 varieties; (8) *Spirochæta obermeieri;* and (9) *Treponema pallidum.*

According to Hartmann, the parasitic Flagellates can be classified as follows:

Phylum:
Protozoa.
Class: MASTIGOPHORA (= whip-bearing organisms).
Order: *Binucleata.*
1. Family: Trypanoplasmidæ.
2. Family: *Trypansosomidæ.*
   (*a*) Leptomonas.
   (*b*) Herpetomonas.
   (*c*) *Trypanosoma.*
   (*d*) *Schizotrypanum.*
   (*e*) Endotrypanum.
3. Family: Halteridæ.

2. Diseases Due to Pathogenic Trypanosomidæ (Human Trypanosomiasis)

Trypanosoma gambiense.—This parasite, the cause of sleeping sickness, was described by Dutton (1901) in trypanosome fever (attention having been earlier called by Forde to the presence of a parasite); it is a small (16–20 μ), fusi-shaped flagellate provided with an *undulating membrane*; it is found in the blood plasma, where it shows active motility and multiplies by fission in the long axis. It is 3 times the length of a red blood corpuscle. In the middle of its body is situated the *principal nucleus*, and at the front end, a *smaller nucleus (blepharoblast)*, whence a long thread runs along the body, *helping to form* the undulating membrane, and passing beyond the sharp *end of the body as a free* flagellum. Resistant forms and resting *forms are now being studied*; they are small round bodies with two nuclei, *and without* flagellum (Moore and Breinle, 1907); these forms are infectious (*Fantham*). Chemotherapeutic experiments indicate that several races exist.

Mode of Infection.—The parasite is transferred to man by the bite of one of the **tsetse flies,** *Glossina palpalis* (Dutton and Todd) (Fig. 98), which is abundant on the banks of streams in Africa, and perhaps also by the bite of *Glossina morsitans*—by the latter especially in high, dry places, by the former in low, damp regions.

Fig. 98.—Glossina palpalis (Tsetse Fly). ×5. (After Dönitz.)

The trypanosomes taken up by the fly undergo a cycle of development in the digestive tract of the insect (Gray and Tulloch, Bruce); sexual forms appear and multiply, becoming infective for man about the third day, and they continue to be infective for at least 75 days (Bruce); it seems probable now, that the fly, once infected, retains the capacity of transmitting the infection for the rest of its life, that is for a year or longer. Only about 5 per cent of the flies ingesting trypanosomes become infected. It is also asserted that the trypanosome can be transferred from one human being to another by sexual intercourse (Koch, Kudicke).

It has recently been found that trypanosomes give rise to specific agglutinins, precipitins, trypanolysins, etc., and that these substances can be used for the differentiation of varieties that closely resemble one another morphologically (Laveran and Mesnil).

Other Trypanosomes.—A number of different species of trypanosomes have been distinguished in **animal infections** (surra, dourine, nagana, etc.). In the Brazilian trypanosomiasis, children suffer from *thyroiditis parasitaria* (Pereira) due to infection with *Schizotrypanum cruzi* (Chagas), transmitted by the insect *Conorrhinus megistus,* or *Triatoma;* and in Rhodesia (Stephens and Fantham), in Nyassaland (Bruce), and in German East Africa (Taute), there is a form of trypanosomiasis, known as *Kaodzera,* due to the *Trypanosoma rhodesiense,* in which the principal

nucleus lies at the posterior end of the body, behind the blepharoblast; the disease resembles that due to *T. gambiense,* and is transmitted by the fly *Glossina morsitans* (Kinghorn and Yorke, 1912), perhaps also by *Glossina brevipalpalis;* 16 per cent of the antelopes in the district harbor the parasite.

(a) *Congo Trypanosome Fever and Sleeping-Sickness*

Definition.—A disease common among the negroes in tropical Africa, known since 1373, attacking also the whites, most prevalent in the region of the Congo and its tributaries, and due to invasion by the *Trypanosoma gambiense* (Dutton) (bite of the fly *Glossina palpalis*). (See above.)

In 1903, at the suggestion of Bruce, Castellani examined the cerebrospinal fluid of negroes suffering from sleeping sickness and found the trypanosome that Dutton had described in trypanosome fever. The disease can be spread only where the tsetse fly exists; this fly can live in certain districts only (wooded banks of streams). The disease is carried from one district to another by infected negroes. Antelopes, cattle and dogs, as well as man, can harbor the Trypanosoma gambiense (Bruce). It is possible that crocodiles also act as carriers of this trypanosome (Koch).

Symptoms.—The incubation period is believed to be 10 to 20 days. The onset is gradual with fever, chills, headache, and vomiting, suggesting a mild malarial attack. Examination of the blood at this stage may reveal the presence of the trypanosomes. The temperature falls in a few days, after which there is a period of well-being lasting several days, or weeks, to be followed by a second febrile attack. Such alternating periods of fever and apyrexia may continue for months (so-called TRYPANOSOMA FEVER). An early and peculiar symptom is hyperesthesia of the deep muscles on pressure. After a time, the patients complain of headache and of pains in the extremities, and the cervical lymph glands become enlarged but not painful (Greig and Gray). In white people erythemas may come and go. Edema of the ankles and about the eyes and cheeks is not uncommon. There is no marked anemia at first, though later in the disease it may be profound. The leukocyte count is low, with relative increase in both the large and small mononuclear elements.

The trypanosome fever, after lasting for months, goes over into true SLEEPING-SICKNESS (invasion of the central nervous system and the cerebrospinal fluid by the trypanosomes). The cerebrospinal fluid shows also an increase in globulin-content. The patients become depressed, apathetic, reminders, mental defects appear, and sensitive epileptiform attacks develop. The patients become lethargic and somnolent. In the more advanced cases, they sleep all the time and can scarcely be awakened for meals, even going to sleep with food in their mouths. Emaciation is rapid, decubitus develops, and death occurs from a complicating terminal septicemia, etc.

The disease may last for years, but appears to be always fatal, once the nervous system has been invaded.

Diagnosis.—This depends upon demonstrating the presence of the trypanosomes in the cervical glands, the blood, or the cerebrospinal fluid. In the stage of trypanosome fever they may be looked for in the fresh blood slide, especially by the dark-field method; a "thick-drop" of blood (Ross, Ruge) will, in stained smears, often show the trypanosomes. They are not numerous, and should, therefore, be looked for repeatedly in many different preparations on successive days.

As soon as the cervical glands become enlarged, gland juice can be obtained by hypodermic puncture, and in this the trypanosomes are often found (Todd).

After the nervous system has become invaded, the trypanosomes can be demonstrated in the cerebrospinal fluid. This fluid shows, as a rule, in sleeping-sickness, an enormous number of lymphocytes (sometimes 1,000-1,200 per c.mm.).

In the differential diagnosis, the disease must be distinguished (1) from *malaria,* and (2) from *relapsing fever;* either of these may complicate a trypanosomal infection.

F. W. Mott has kindly shown me specimens from the brain of patients dead of African sleeping-sickness; the perivascular infiltration with small mononuclear cells is very striking.

(*b*) *Rhodesian Trypanosomiasis* (*Kaodzera*)

Definition.—A disease prevalent in Rhodesia, similar to the trypanosome fever and sleeping-sickness due to *Trypanosoma gambiense,* but due to a different parasite, *Trypanosoma rhodesiense* (Stephens and Fantham), and showing certain epidemiological peculiarities.

Occurrence.—Discovered in Rhodesia (1910), the disease has also been observed in Nyassaland (Bruce), in Portuguese East Africa, and in German East Africa (Taute).

Symptoms.—These are similar to ordinary sleeping-sickness, but the disease is more virulent and progresses more rapidly. The *incubation period* lasts 5-10 days, and the course is rapid, averaging 4½ months. The parasites are often present in large numbers in the blood. The lymph glands may not be enlarged. The three stages of the disease are well described by Shircore.

(*c*) *Brazilian Trypanosomiasis* (*Chagas' Disease; Thyroiditis parasitaria; Careotrypanosis*)

Definition.—An endemic, acute and chronic disease due to *Schizotrypanum cruzi,* occurring among children, in the interior of Brazil, apparently related to the parasitic thyroiditis prevalent there; the parasite is introduced by the bite of an insect (see above).

Symptoms.—In the *acute forms,* small children under 1 year are affected during the hot months (October to March). They sicken with high fever and enlargement of the lymph glands, spleen and liver. Trypanosomes can be demonstrated in the blood, for from 10 to 30 days, after onset. The thyroid becomes enlarged and

signs of infantile myxedema develop (skin, bradycardia). In the severer cases signs of meningo-encephalitis develop, and the patients die, or, if they recover, suffer from organic nervous lesions.

In the *chronic forms* it may not be possible to demonstrate the parasites on microscopic examination of the blood, except during exacerbations, though they can be recovered by inoculating a guinea-pig with the blood of the patient. The heart muscle is often invaded.

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2. Diseases Due to Varieties of Leishmania (Human Leishmaniasis)

Varieties of Leishmania.—These parasites are *Protozoa,* class *Mastigophora,* order *Binucleata,* family *Piroplasmidæ,* species *Leishmania.* Three varieties are known to invade human beings: (1) *Leishmania donovani,* causing kala-azar; (2) *Leishmania infantum,* causing infantile leishmaniasis; and (3) *Leishmania furunculosa sive tropica,* causing oriental sore, or cutaneous leishmaniasis.

Leishmania donovani.—This protozoön appears in the form of small ovoid corpuscles (2-4 μ) with two characteristic nuclei, one main nucleus, rounded, the other, accessory nucleus, oblong or rod-shaped (Plate VIII, Fig. 2). These corpuscles are usually enclosed in macrophages (endothelial cells, large mononuclear leukocytes); they are occasionally seen in polymorphonuclear neutrophils and in eosinophils but never in lymphocytes or in erythrocytes (Patton).

They undergo bipartite subdivision occasionally, dividing into four. Close to the accessory nucleus, can sometimes be seen a rhizoplast, or flagellum-root. In isotonic solutions of sodium citrate, or on McNeal-Novy-Nicolle agar-medium, these corpuscles grow out, in a few days, into small club-shaped flagellates (L. Rogers, 1904). These parasites differ from trypanosomes, in that the flagellum is formed at the posterior end directly from the blepharoplast (accessory nucleus) out of the rhizoplast, and no undulating membrane is formed. In nature, a similar development into flagellates appears in the intestinal canal, in the bed-bug, and perhaps

in other insects (fleas, flies). The parasite is pathogenic for monkeys (Row). Spontaneous infection of cats and dogs rarely, if ever, occurs (in contrast with L. infantum).

(*a*) *Kala-Azar*

(Tropical Splenomegaly, Dum-Dum Fever, Cachectic Fever)

Definition.—A tropical disease, characterized by enlargement of the spleen and liver, progressive anemia, and outspoken cachexia, due to invasion with *Leishmania donovani* (R. Ross).

It is common in India, having been known there since the English observed it in 1869, but occurs also in China, Arabia, Egypt, Algiers, Italy, Greece, and Portugal. In Assam, over 26 per cent of the population is infected before the tenth year, 50 per cent or more by the twentieth year (Clarke and McNaught; L. Rogers). The disease was supposed to be a form of malaria until Leishman (1903) discovered the parasite in spleen cells. His observation was confirmed by Donovan and others, and soon examinations for the parasite were used for the diagnosis of clinical kala-azar (Bentley, Christophers, L. Rogers). The disease is probably transmitted by an insect, *Clinocoris rotundatus* (Patton, 1907, 1912), or, possibly, by *Conorrhinus rubrofasciatus* (Donovan).

Symptoms.—The *incubation period* lasts about 20 days, but may be longer. The disease is characterized by (1) splenic tumor, the spleen often extending to the umbilicus; (2) irregular fever (two elevations every 24 hours); (3) progressive anemia; and (4) an extraordinary leukopenia (L. Rogers). In 90 per cent of cases, there are less than 3,000 W. B. C.; in 40 per cent less than 1,000. Leishman described three stages of the disease: (1) initial stage; (2) febrile stage with splenomegaly; and (3) cachectic stage.

The course is chronic (6-18 months); more acute and more chronic forms also occur (3 months; 10 years). The mortality is about 98 per cent without treatment; with treatment it can be reduced to 70 per cent.

Diagnosis.—The parasites can sometimes be demonstrated (Leishman's, Wilson's, or Giemsa's stains) in the leukocytes in blood smears; 5-30 are present in a smear from 73.2 per cent (Donovan) to 86.8 per cent (Marshall) of advanced cases; in one instance, Patton found 1,043 in a single smear. Diagnosis by the blood smear, however, is often difficult. It is much easier to demonstrate the parasites in smears of splenic juice (dry, sterile syringe!), but great care should be taken in splenic puncture (q. v.). Some puncture the liver for diagnosis, as there is less danger of hemorrhage. Others examine the bone-marrow of a rib or trephine the tibia Occasionally, a cutaneous ulcer is present, and smears from it reveal the parasites. The parasites occur in ulcers of the intestine (Manson and Low); in one instance they were found in mucus in the feces (Rach and Zarfl). Novy recommends blood cultures (10 c.c. blood) on N. N. N. agar, for diagnostic purposes.

In *advanced cases,* the cachexia, the earthy color, the splenomegaly, and

the enlargement of the liver are characteristic. In *early cases*, the marked leukopenia should excite suspicion.

Differential Diagnosis.—The disease has to be differentiated (1) from *malaria;* (2) from *Banti's* disease; (3) from *other forms of splenomegaly* (q. v.); (4) from *Malta fever;* and (5) from *typhoid* and *paratyphoid.* The important thing is to *think* of the possibility of kala-azar.

(*b*) *Infantile Kala-Azar or Infantile Leishmaniasis*

The *Leishmania infantum* of Nicolle, which causes infantile kala-azar of Tunis, Southern Italy, and the shores of the Mediterranean Sea generally, attacks children rather than adults, causing anemia and splenomegaly. Dogs, cats and monkeys are susceptible. Fleas (*Pulex irritans, Pulex serraticeps*) appear to transmit the disease (Basile, Visentini). The parasite differs somewhat from that of the kala-azar of adults; it grows much more easily on N. N. N. agar (Nicolle). Dogs can be infected experimentally (Novy). Clinically, there is enormous enlargement of the spleen, emaciation and cachexia; there may be severe diarrhea at the beginning. There is leukopenia and moderate anemia (Jemma, Cannata, di Christina). It is much more difficult to find the parasites in blood smears than in kala-azar of adults, though by long search they are found; Cannata demonstrated them in 7 out of 8 cases.

Fig. 99.—Oriental Sore. (After S. T. Darling, Arch. Int. Med.)

(*c*) *Cutaneous Leishmaniasis or Oriental Sore*

(*Leishmaniasis cutanea, Bouton d'Orient, Delhi Boil, Bouba, Utah*)

Leishmania tropica.—This flagellate, discovered by J. Homer Wright (1902), differs slightly from the parasites of kala-azar. Nicolle first grew it on N.N.N. agar. It is the cause of Delhi boil.

The disease can be transferred to man by inoculation (Depérer and Boinot, 1884), and to dogs and monkeys (Nicolle and Manceaux).

The disease has been given various names, including *Aleppo boil, Bagdad sore, tropical sore,* etc. This skin lesion is widely distributed throughout the world; recently it has been shown to exist in a severe form in Brazil, Peru, and Paraguay. The lesions are often multiple as in the *"Espundia"* of Peru, the *"Bouba"* of Brazil and Paraguay, the *"Utah"* of Peru (Strong, Tyzzer and Sellards). Ulcers on the exposed parts of the body appear, most often at the end of summer, and in the early autumn (insects.). Sections and smears of the ulcer show the presence of *Leishmania*

tropica. Occasionally, the parasites can be seen in the blood, or in regional lymph glands. The disease is a less virulent type of leishmaniasis than the two preceding varieties. In the South American form, a severe buccopharyngeal localization is sometimes seen. The disease in South America is often confused with framboesia (yaws).

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3. Human Malaria

Parasites of Malaria.—These plasmodia lead their vegetative existence upon red blood corpuscles. They show an alternation of generations, the ASEXUAL PROPAGATION (schizogony) being carried on in the blood of the intermediate host (man), the SEXUAL PROPAGATION (gamogony or sporogony) being carried on in the gastro-intestinal canal of the definitive host (mosquito). The *malarial diseases,* as Laveran discovered, are due to such parasites (malarial parasites), of which there are at least three varieties (*vide infra*). These malarial parasites belong to the Family *Plasmodidæ,* of the Order *Binucleata,* of the Class *Mastigophora,* which is one of the great groups of *Protozoa* (cf. Prowazek).

LIFE HISTORY OF MALARIAL PARASITES.—In the accompanying figure (Fig. 100), the development of these parasites is schematically illustrated. According to the description given by Claus Schilling, the youngest forms, or the *merozoites* (1) penetrate the red corpuscles and begin to grow there. In the plasmodium, a nutritive vacuole soon appears which gives the protoplasm a ring-shaped appearance. As the plasmodia grow larger (2, 3, 4) pigment is formed. In the full-grown parasite, the red corpuscle may be almost entirely filled by the plasmodium (5). The vacuole disappears; the pigment increases. The parasite is now ready to undergo segmentation, the whole period of growth requiring, for the tertian and for the estivo-autumnal parasites, about 48 hours, and for the quartan parasite about 72 hours. A "*segmenter*" (6) is a parasite undergoing subdivision into a large number of merozoites. In the case of a tertian parasite, there are 15-25 segments; in the quartan parasite, 6-14, usually 8; and in the estivo-autumnal parasite, 8-25. These small merezoites invade as yet unaffected red corpuscles (1) and the cycle (*schizogony*) is gone through again. The pigment is engulfed by phagocytes and is carried to the spleen and liver.

In addition to the schizontic forms, *sexual forms,* or *gametes,* also appear (7, 12). They are distinguishable from schizonts in that they contain no vacuoles, and in that, even when very small, they contain pigment. The *male gametes,* or so-called microgametocytes (12, 13, 14) possess a rather homogeneous protoplasm and abundant nuclear material, in contrast with the *female gametes,* or macrogametocytes (7, 8, 9), in which the protoplasm is granular and the nuclear material less evident. These sexual forms grow more slowly than the schizonts. In the estivo-autumnal form, they assume the form of "ovals" and "crescents."

The female sexual forms (macrogametocytes) are capable of undergoing, without fertilization, a process of segmentation (11) following upon nuclear reduction (10), with formation of merozoites, which again start a new schizogonic cycle (1).

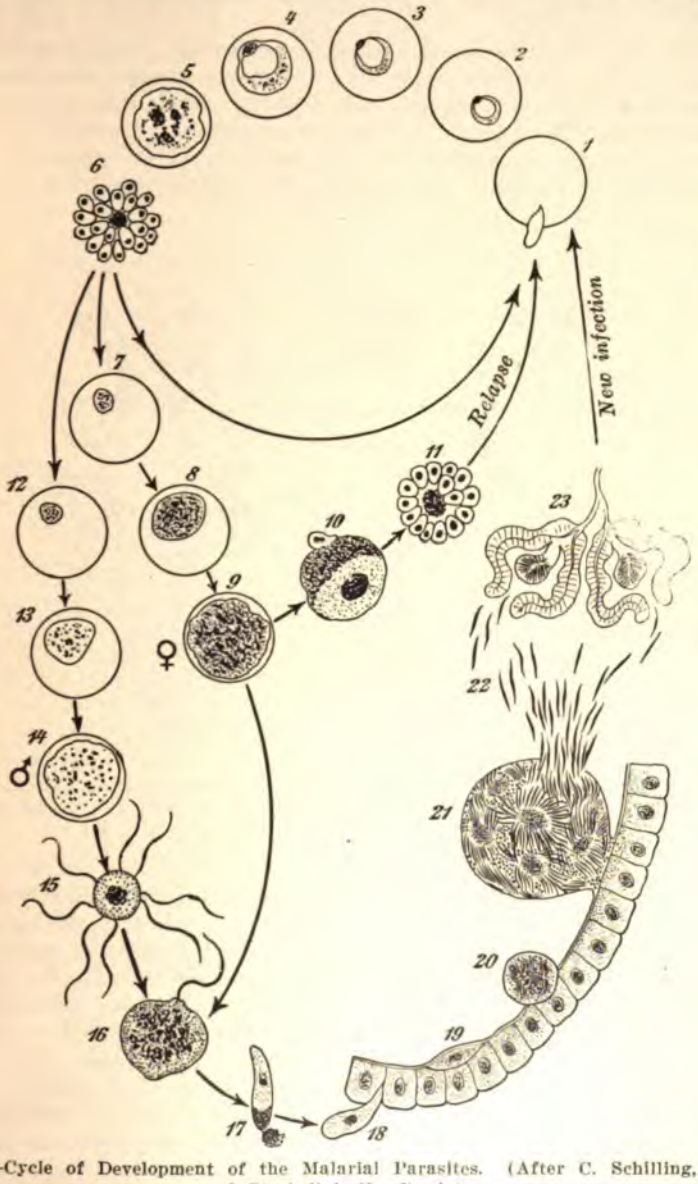


Fig. 100.—Cycle of Development of the Malarial Parasites. (After C. Schilling, in Mohr & Staehelin's Handbuch.)

It is such *parthenogenetic reproduction*, by macrogametocytes that accounts for *latent infections* with malaria, and, under certain circumstances *relapses* may be thus started, especially in the spring of the year, or on removal of the patient from one climate to another. The gametes are resistant, latent forms.

Now it is the gametocytes (micro and macro) which start the *sexual cycle* (sporogony) in the gastro-intestinal canal of mosquitoes. The *Anopheles* appears to be the only species of mosquito in which this cycle occurs. But not every species of Anopheles acts as a carrier. Thus in India, it has been found that *Anopheles rossi* is unimportant, while *Anopheles christopheri* is a very important host.

It is the "female of the species" which is concerned. Biting a patient whose blood contains male and female gametes, remarkable changes take place in the swallowed blood. The microgametocytes undergo what was formerly called *flagella-formation.* The pigment becomes concentrated, the nucleus divides into 8-10 parts, which become arranged in the periphery of the plasmodium. Suddenly, threadlike projections emerge from the surface (so-called *flagella;* in

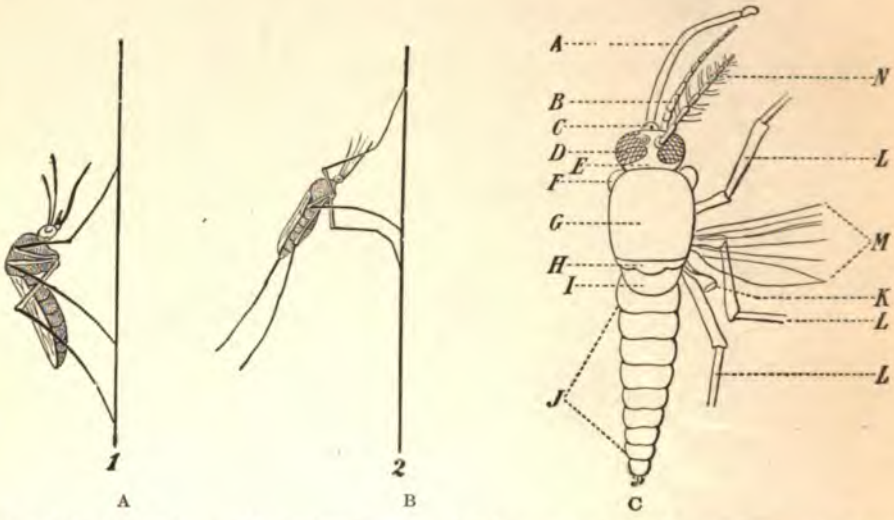


Fig. 101.—Mosquitoes. (A) Resting Position of Culex on Vertical Surface, (B) Resting Position of Anopheles on Vertical Surface, (C) Diagram of Typical Anophelina. (After C. F. Craig, "Malarial Fevers," published by Wm. Wood & Co., N. Y.)

reality, *microgametes*). They consist chiefly of nuclear substance with a little protoplasm (15), are actively motile, and become separated from the parent body, which retains the pigment. They migrate as minute, snakelike bodies, among the red blood corpuscles, until they find a macrogamete (9) that has undergone reduction division and is ready for fertilization. A minute spermatozoonlike microgamete penetrates the macrogamete at an elevated spot, the so-called *fertilization hillock* (16) and fertilization (anisogamia) takes place. The fertilized macrogamete, or *zygote,* soon changes into a wormlike structure called an *oökinete* (17). This casts off the pigment, penetrates the wall of the stomach of the mosquito, passing between the epithelial cells (18), and comes to lie in the outer wall of the stomach (19), where it grows into a larger vesicle known as an *oöcyst* (20). In this, there gradually develop a large number of extremely minute, spindle-shaped germs, each containing chromatin material (21). The cyst wall ruptures and the minute germs are emptied into the body cavity of the mosquito (22). These small sickle-shaped germs are known as *sporozoites.* They

PLATE V

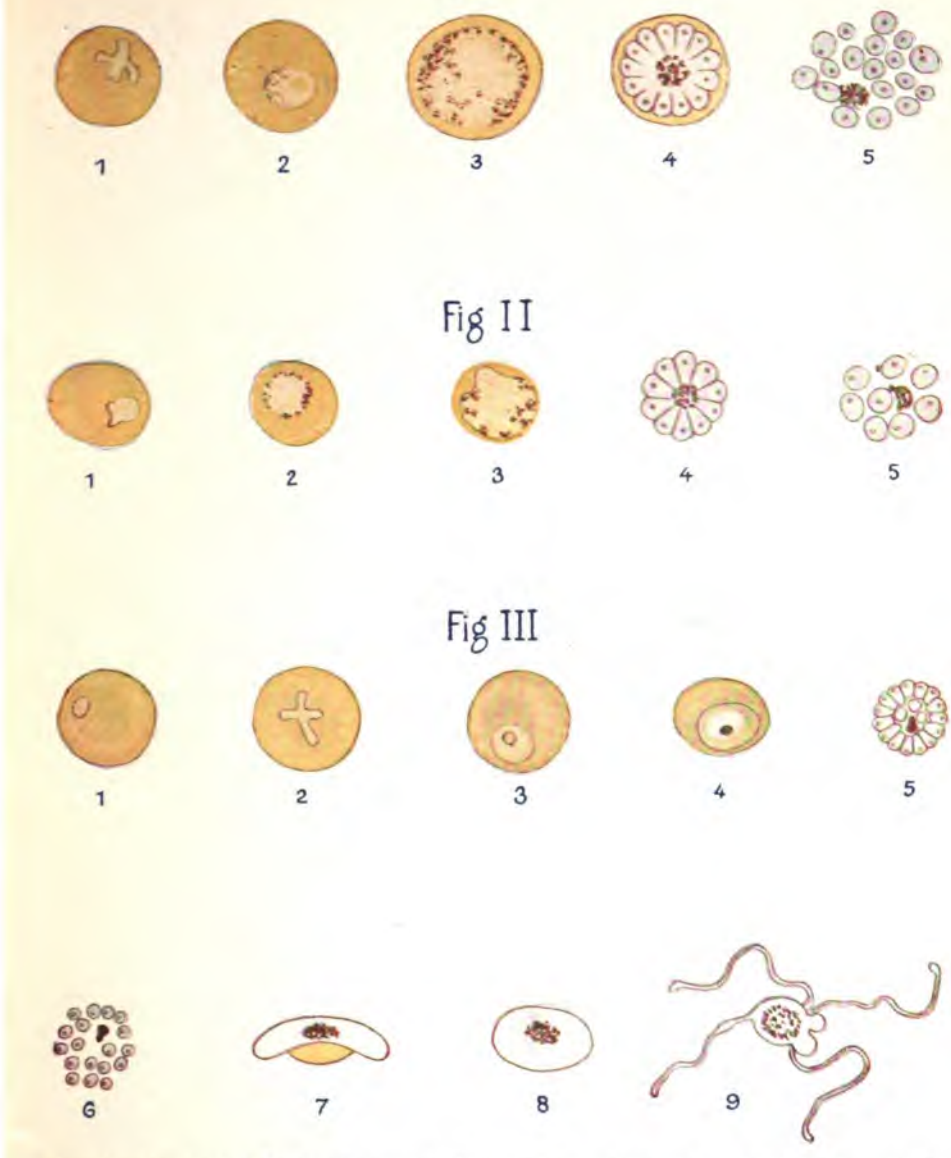


Fig. 1.—Parasites of Tertian Fever: (1) Young Hyaline Forms, (2) Beginning Pigmentation, (3) Full Grown Bodies, (4 and 5) Segmenting Bodies.

Fig. 2.—Parasites of Quartan Fever: (1) Young Hyaline Form, (2 and 3) Developing Within the Corpuscle, (4 and 5) Segmenting Bodies.

Fig. 3.—Parasites of Aestivo-autumnal Fever: (1) Small Refractive Ring-like Body, (2) Larger Disk-like and Ameboid Form, (3) Similar Pigmented Body, (4) Segmenting Body, (5) Ovoid Form Segmenting, (6) Segmenting Parasite, (7) Crescent Form, (8) Vacuolization of a Crescent, (9) Flagellating Form. (After Thayer & Hewetson's "Malarial Fevers of Baltimore." J. H. H. Rep.)

now wander through the body to the salivary gland in the neck of the mosquito, penetrate the gland cells, and appear in large numbers in the ducts of this gland (23). When a mosquito so infected bites a human being, the contents of the salivary gland are injected into the wound, and the human being becomes inoculated with the sporozoites. These enter the red corpuscles and start a schizogonic cycle. The **alternation of generations** is thus completed, the asexual cycle in the human body (schizogony), and the sexual cycle (gamogony, or sporogony) in the body of the definitive host, the Anopheles mosquito.

(*a*) *Tertian Malaria*

Plasmodium vivax (*Grassi and Feletti*).—This parasite is best studied in fresh blood, and in smears stained by Giemsa's or Wilson's stain. The young forms appear as small rings, in diameter about $\frac{1}{6}$ that of a white blood corpuscle. One-half of the ring is thicker than the other (*seal-ring form*), but the red chromatin granule lies in the thinner half. At the end of 24 hours, the rings fill about $\frac{3}{4}$ of the corpuscle and contain dark brown granules of pigment. The fresh blood slide, at this stage, shows active ameboid movement and vacuolation of the parasite. The vacuole soon grows smaller. At the end of 48 hours it has disappeared. The infected red blood corpuscle is now markedly enlarged ($1\frac{1}{2}$ times its normal size), the parasite containing actively dancing, yellowish-brown, pigment-granules. The red corpuscle shows a fine stippling of a brick-red color (Plate VII, Fig. 1) in well-stained specimens (Schüffner's stippling), not met with in other malarial infections. Segmentation occurs at the end of 48 hours, each of the 15-25 segments containing nuclear material. (Plate VI, Fig. 1.)

The gametocytes contain no nutritive vacuole, and are more pigmented than the schizonts. When half-grown, the male cells have a clear protoplasm and relatively little chromatin, while the female cells have a dark granular protoplasm and relatively little loose-meshed chromatin. When full-grown, they are $1\frac{1}{4}$ to $1\frac{1}{2}$ times the size of a red blood corpuscle.

(*b*) *Quartan Malaria*

Plasmodium malariæ (*Grassi and Feletti*).—During the first 24 hours of its development, this parasite looks very much like the tertian parasite. As it grows older, it tends to form an *oblong band* across the red blood corpuscle. The pigment is blacker than that of the tertian parasite, and the red blood corpuscle in which the parasite is contained, instead of enlarging, contracts somewhat, is crenated, and has a brassy color. The quartan parasite is less ameboid than the tertian, and soon loses its nutritive vacuole. On segmentation, it gives rise to only 6-12 merozoites, which arrange themselves in rosette-form around a pigmented center. At 60 hours, the quartan parasite is about the size of a red blood corpuscle. Segmentation occurs at the end of 72 hours. (Plate VI, Fig. 2.)

of malaria, with 2 million deaths, at least double the yearly average. Dr. Edwin C. Cort tells me that he has observed similar fatal epidemics in Northern Siam.

Symptoms.—The incubation period lasts from 1 to 3 weeks. The onset is sudden, after slight premonitory symptoms, with severe CHILL, chatter-

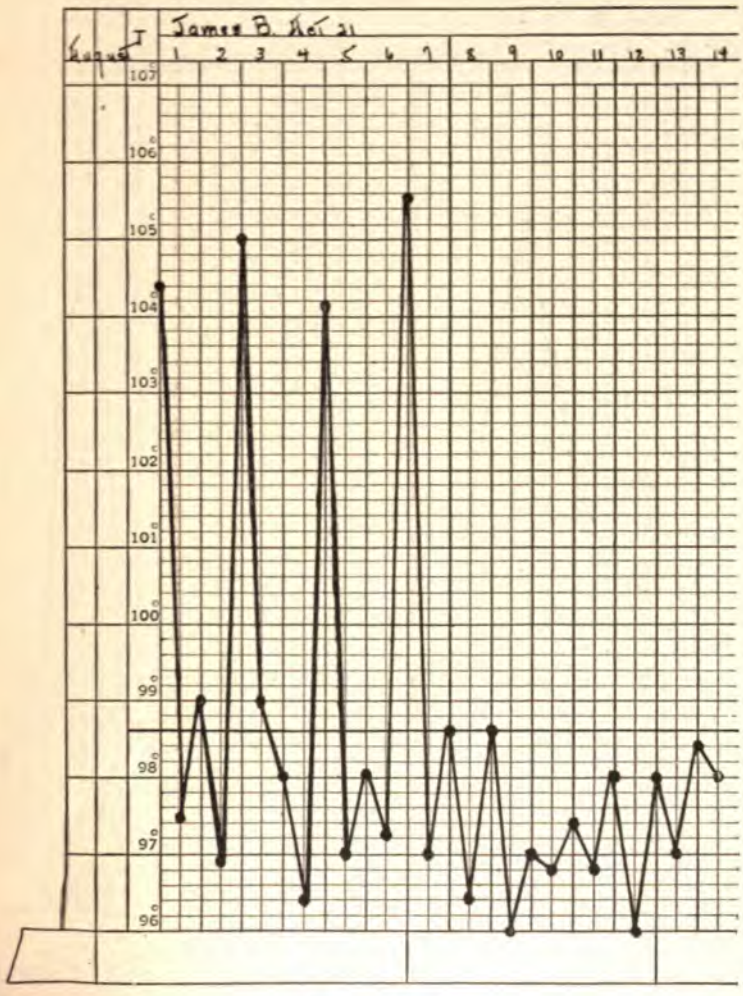


Fig. 102.—Tertian Malaria.

, headache, palpitation, cyanosis, goose-skin, livid nails, and vomiting, small, frequent hard pulse, and rapid rise ften to 105° or 106° F. The chill lasts for from 1 to 3

hours. The feeling of cold then gives way to a feeling of burning HEA (2 to 4 hours), during which the face is red, the skin hot and dry, the r piration rapid and superficial, the pulse large and soft. The patient restless, thirsty, nauseated, complains of headache, and perhaps is slight

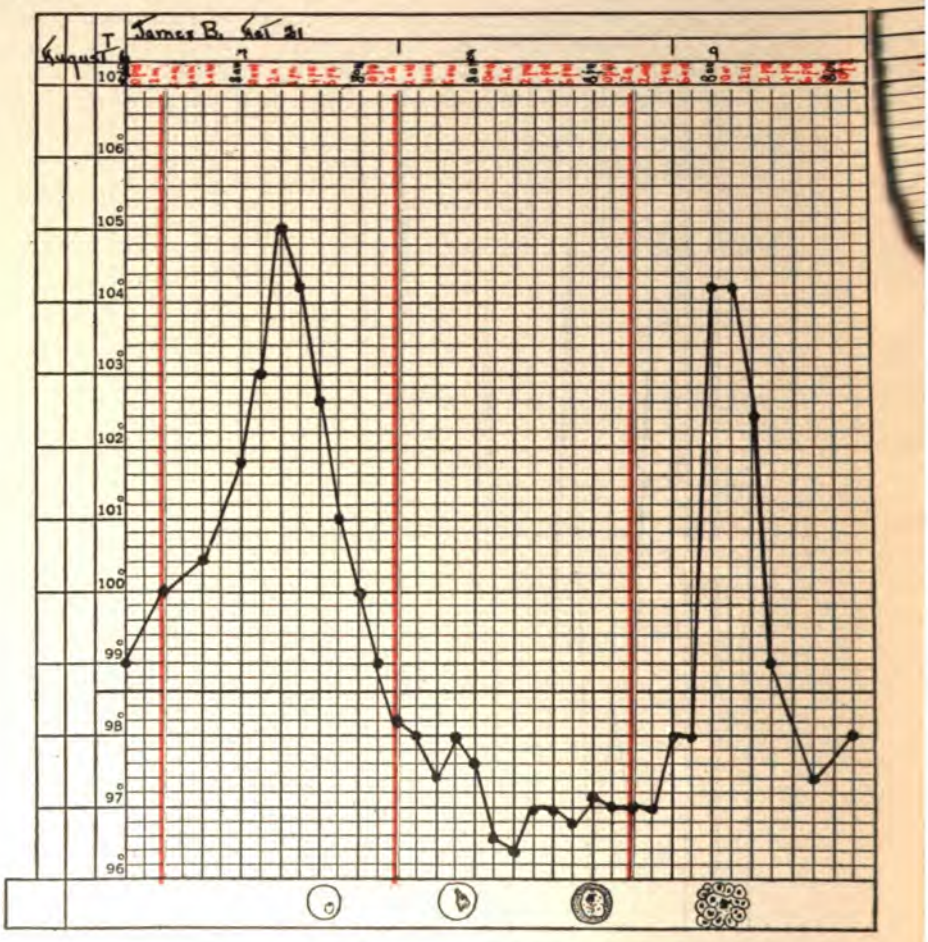


Fig. 103.—Two-Hourly Chart of Tertian Malaria.

delirious; after this the temperature falls suddenly to normal or subno and the patient breaks out into a profuse SWEAT. Such an attack (*m paroxysm*) lasts altogether from 7 to 10 hours, and corresponds time of maturation and segmentation of a generation of parasit blood. After the sweating, say from 12 to 18 hours after the onse

attack, the patient is greatly relieved and says that he feels well again, though he may be weak.

In a single infection with *tertian malaria,* a generation ripens every 3rd day (TERTIAN FEVER). In a single infection with *quartan malaria,* a generation ripens every 4th day (QUARTAN FEVER). In single infections

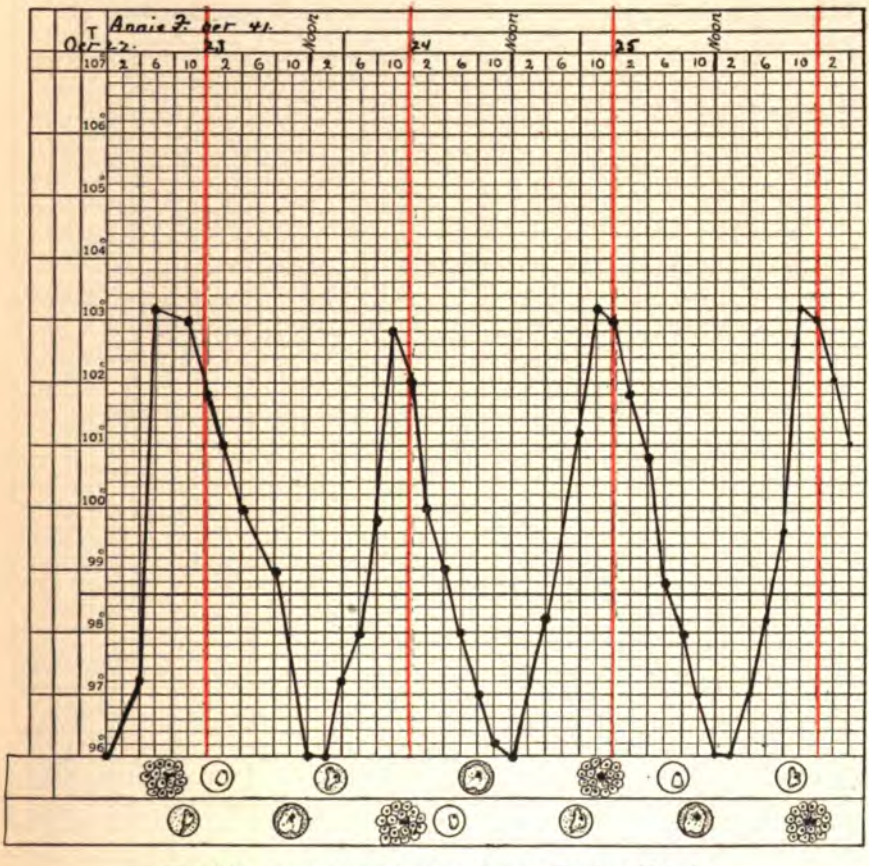


Fig. 104.—Two-Hourly Chart. Double Tertian Malaria.

with the *estivo-autumnal malaria,* the attacks usually occur every 3rd day. In *double tertian* or *triple quartan* infections, a generation of parasites may mature daily (QUOTIDIAN FEVER). In estivo-autumnal fever, there are often many generations of parasites so that some segmentation is going on all the time (CONTINUOUS MALARIAL FEVER); in the latter instance, the course of the fever may resemble that of typhoid. Chills are often absent, the paroxysms of fever are longer than in tertian fever, lasting usually

ver 20 hours, frequently with a more gradual ascent and descent of the emperature than in the other forms.

The spleen soon becomes palpable and increases in size if the attacks ontinue. The liver is sometimes enlarged. Herpes labialis is common,

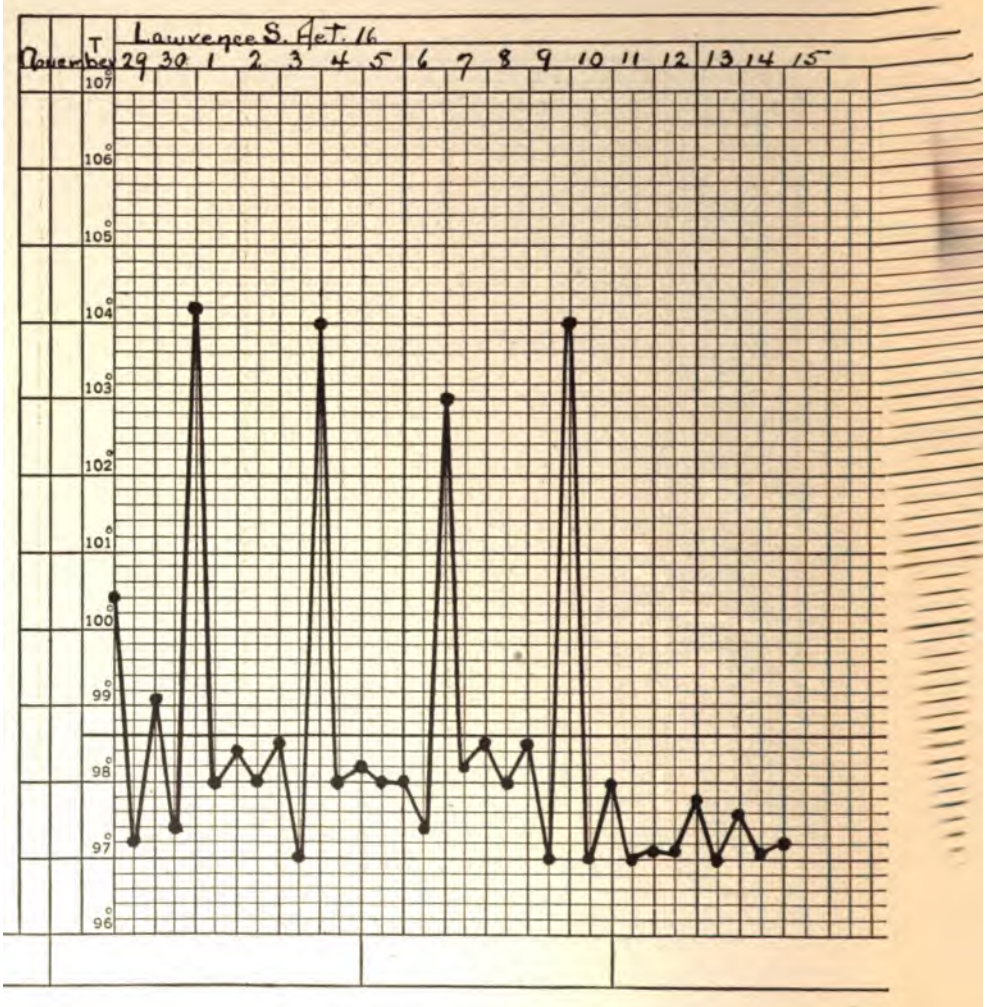


Fig. 105.—Quartan Malaria.

s is also miliaria crystallina. Leukopenia is constant, except durir aroxysm, when there is sometimes a slight leukocytosis. In latent a ions, neuralgia may be a symptom.

In estivo-autumnal fever of the PERNICIOUS TYPE, severe and

fatal cerebral symptoms (*malaria cerebri*) or intestinal symptoms (*choleriform malaria*) may occur, due to thrombosis of capillaries with enormous numbers of infected red corpuscles.

In long continued malaria the so-called MALARIAL CACHEXIA may develop (grave anemia, pigmented skin, edema, enlarged firm spleen or "ague-cake," hemorrhagic diathesis, secondary infections).

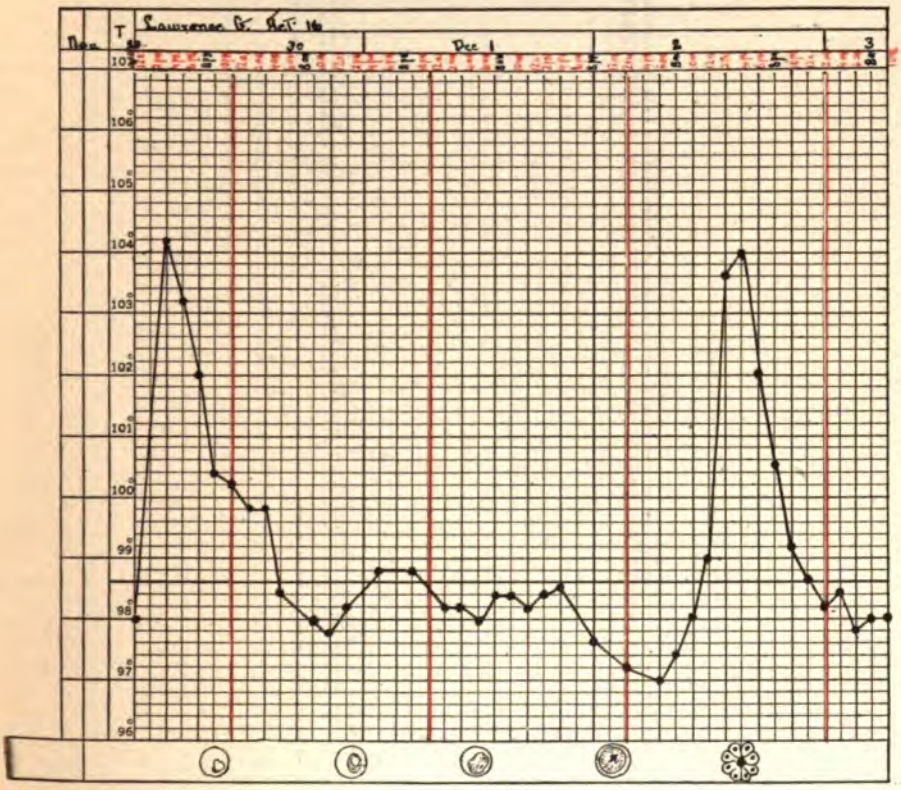
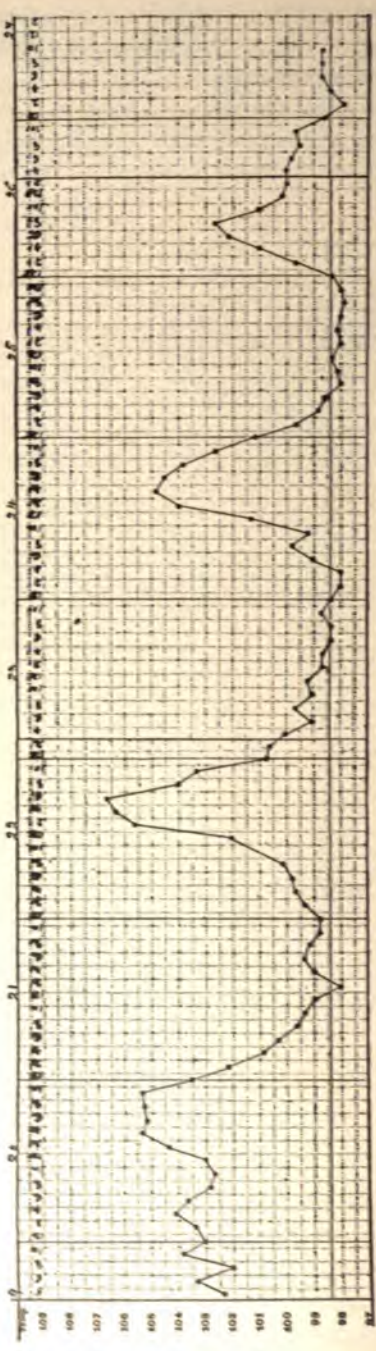


Fig. 106.—Two-Hourly Chart Quartan Malaria.

Diagnosis of Malaria.—This is easy, if malaria be thought of and the blood be searched for parasites (fresh, and stained, specimens). The leukopenia helps to rule out ulcerative endocarditis and other septic processes, accompanied by intermittent fever. In the differential diagnosis, a negative blood culture helps to rule out *typhoid fever*. The "therapeutic test" with quinin rules out *fevers other than those of malarial origin*. The absence of early jaundice, the presence of marked splenic enlargement, and



7.—Chart of Malarial Fever, Estivo-Autumnal Tertian.
(After W. S. Thayer, J. H. H. Bull.)

arasites in the blood rule out *yellow fever*. Dysentery, nephritis, and e tropics, sleeping-sickness, and relapsing fever may have to be con- ed in the differential diagnosis. In the United States the irregular

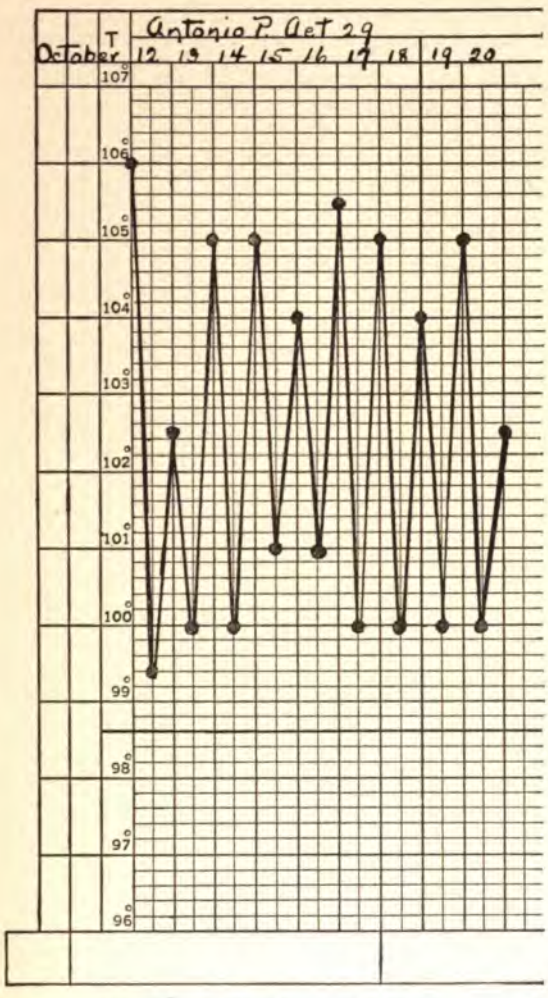


Fig. 108.—Estivo-Autumnal Malaria.

of tuberculosis is often supposed by patients, and even by physicians, malarial! The fever of *syphilis* is sometimes confused with malarial

Black-water fever is a malarial fever, associated with hemoglobinuria,

depending upon a hemolytic process, the exact nature of which is at nt obscure. (See Diseases of the Blood.) Some have thought that n plays a part in giving rise to the hemolysin. (See Part VII.) Considerable EXPERIENCE IN EXAMINING BLOOD is necessary for pro- ncy in malarial diagnosis. Unskilled observers often report a positive

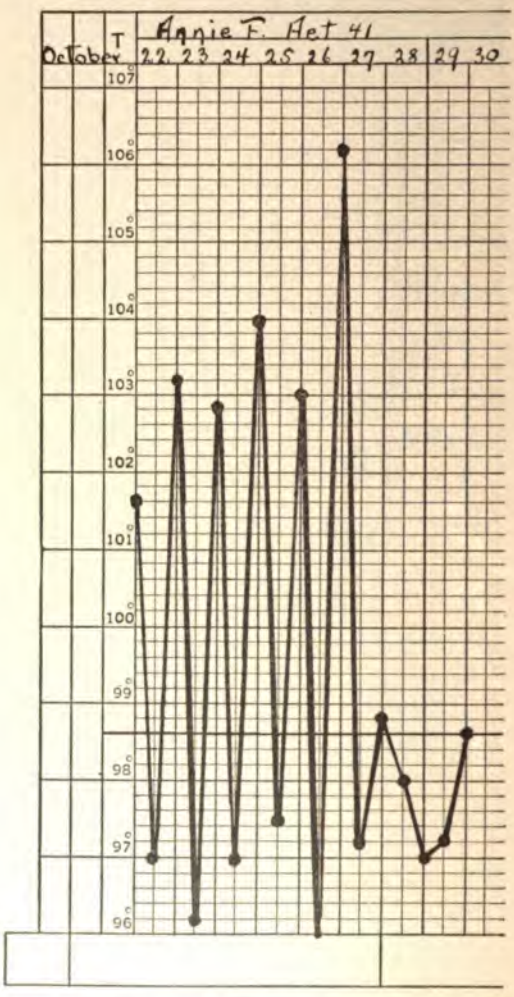


Fig. 109.—Quotidian Malaria. (Double Tertian.)

ng when no parasites are present, and they often overlook parasites they are actually there. Occasionally, when no parasites are found, of pigment-containing leukocytes identifies the nature of the

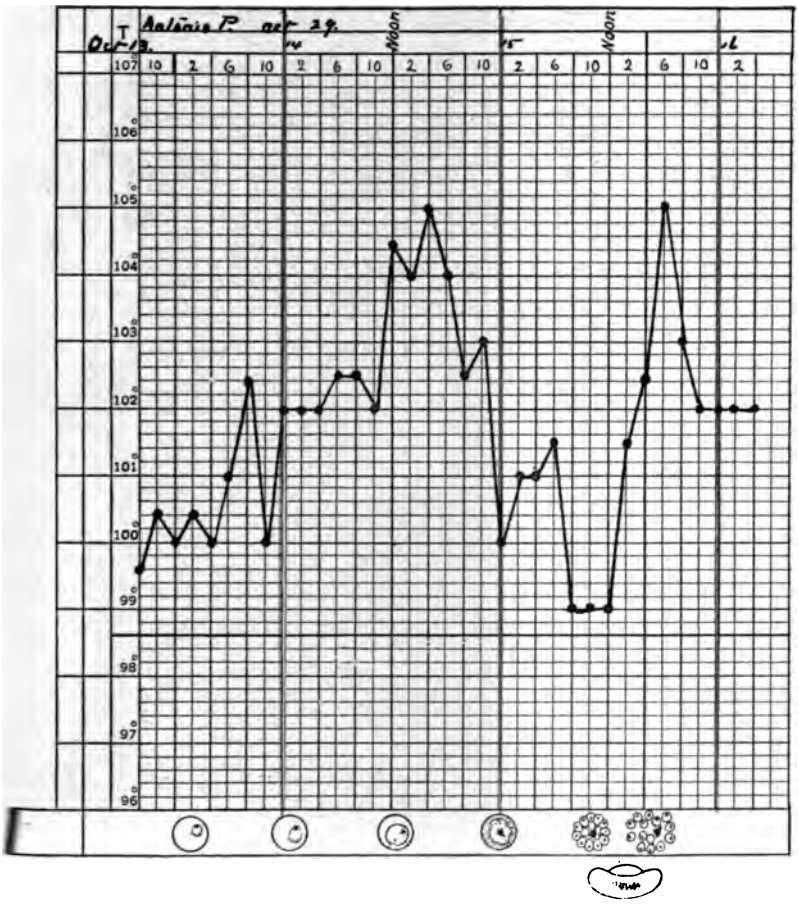
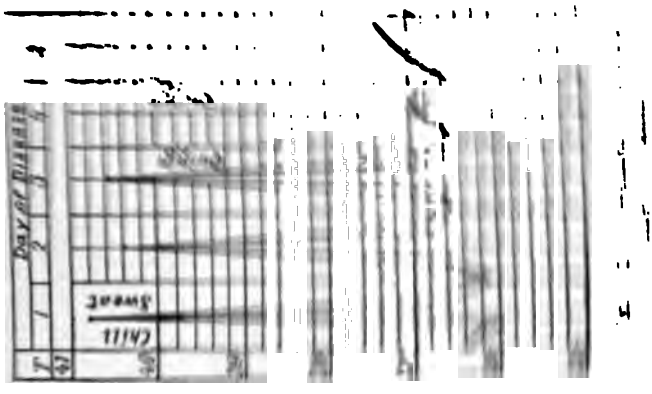


FIG. 110.—Temperature Chart of Malarial Fever. (Estivo-Autumnal Four-Hourly Chart.)


Chill
Sweat

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4. Relapsing Fever

(*Febris recurrens*)

Spirochæta obermeieri.—In relapsing fever, a flagellate of spirochaeta form, was first discovered by Obermeier (1868). His publication on the subject (1873) was the first report demonstrating the presence of a pathogenic microörganism in human beings.

The *Spirochæta obermeieri* is a corkscrew-shaped spirochaete (10-40 μ long), which undergoes screwlike movements in the infected blood, shoving the corpuscles about in the fresh preparation. The spirochaetes can be kept alive in blood serum for over 100 days. The disease can be transferred from man to monkeys, and from monkeys to rats and mice.

In the relapsing fever of different countries, somewhat different varieties of spirochaetae have been found; thus the European relapsing fever is due to *Spirochæta obermeieri,* the African to *Spirochæta duttoni,* the American to *Spirochæta novyi,* the Indian to *Spirochæta carteri.*

Fig. 112.—Spirochetes of Relapsing Fever from Blood of a Rat Seen at the Height of the Infection, Showing One Normal Double Form (A), One Stretched Out Form (B), and One Recurved Form (C), in One Cover-Slip Preparation. (After S. T. Darling, Arch. Int. Med.)

Definition of Relapsing Fever.—Relapsing fever is an infectious disease characterized by periods of fever separated from one another by periods of apyrexia, and due to invasion of the blood by one of several varieties of spirochaetae. The incubation period lasts about 7 days.

Fig. 113. — Ornithodorus Moubata. ♀ The Tick that Transmits Relapsing Fever. (After G. H. F. Nuttall, J. H. H. Bull.)

Mode of Infection.—Infection probably occurs through bloodsucking insects, of which the louse (*Pediculus vestimenti*) seems to be responsible in Algiers, a tick (*Ornithodorus moubata*) in equatorial Africa. Simple contact infection seems improbable.

Symptoms.—The onset is with fever, and usually with chill, headache, pain in the back, tinnitus, general malaise, pain in the calves and in the extremities generally. The

ngue becomes coated. Herpes is not uncommon. Constipation, vomit-
ig, splenic tumor, moderate leukocytosis, with slight relative increase in
ie polymorphonuclear elements, are also usually present.

The fever continues high for 5-7 days, and then falls by crisis, with
weating and diarrhea; there is then rapid disappearance of the symptoms.

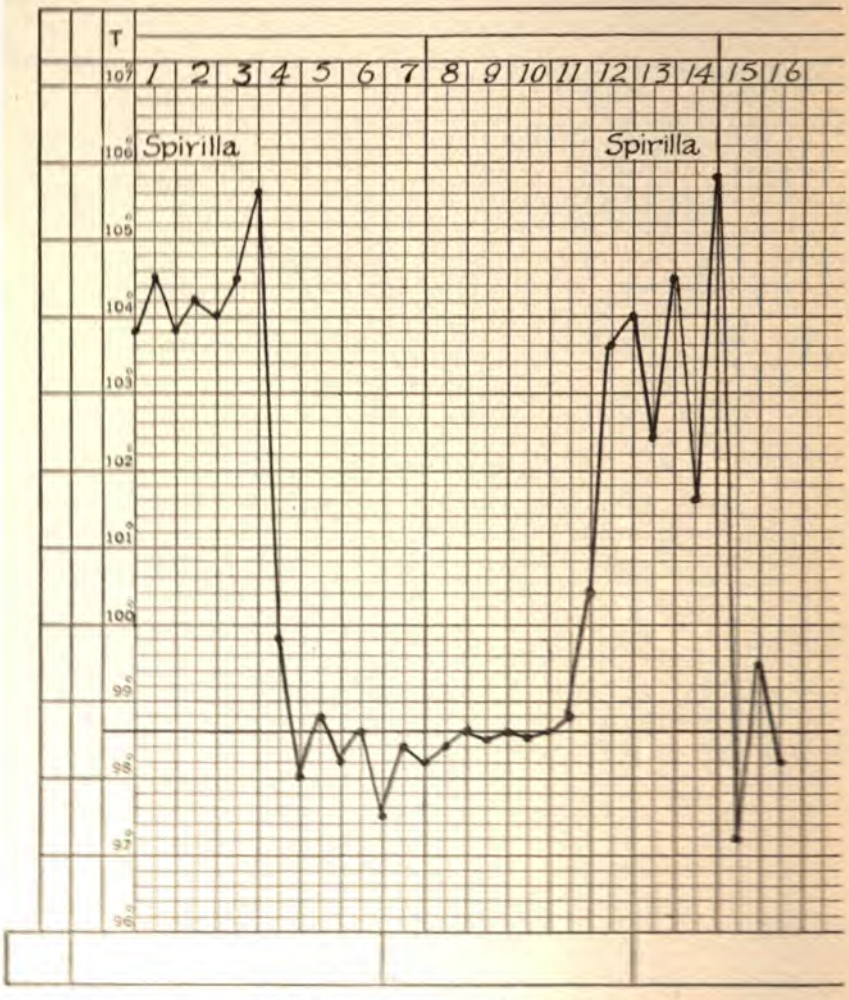

Fig. 114.—Relapsing Fever. (After P. Krause.)

: nearly all cases, after an interval averaging 5½ days (but sometimes as
reat as 17 days), a RELAPSE, wholly similar to the first attack, except
iat it is milder, occurs. The average duration of the first attack is 6¾
ays, of the second attack, 5½ days. In most cases, the disease is over at the
id of the second attack, but in about 7 per cent of the cases, a SECOND

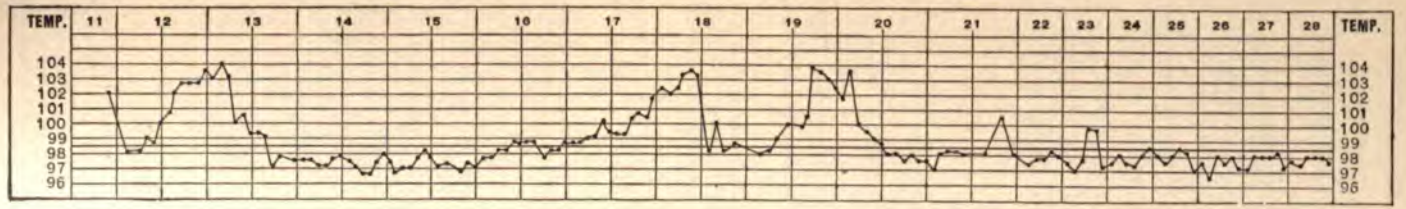

Fig. 115.—Course of a Case of Relapsing Fever of Panama. (After S. T. Darling, Arch. Int. Med.)

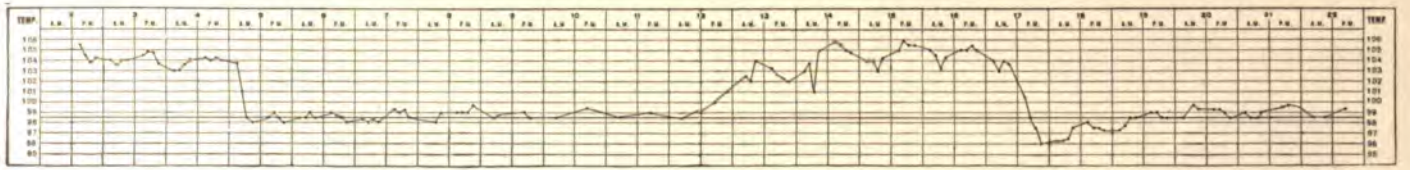

Fig. 116.—Course of a Case of Relapsing Fever of Europe. Note Sustained Temperature During Paroxysm and the Prolonged Duration of Same. (After S. T. Darling, Arch. Int. Med.)

RELAPSE occurs 6 days later, lasting on the average 3¼ days. In a few cases, a THIRD RELAPSE comes after a 9 days' intermission and lasts 2 days, and even a FOURTH RELAPSE (after 10 days' intermission) lasting 1 day, has been observed.

In rare instances, during the apyretic period following the first attack, an intense jaundice sets in (septic bilious recurrent fever, or bilious typhoid). This appears to be a complication due to pyogenic sepsis. The average mortality of relapsing fever is from 2 to 10 per cent. One attack does not confer immunity to subsequent infection.

Diagnosis.—It is often difficult to demonstrate the spirochaetae in the peripheral blood, especially at the height of the fever, though the thick-drop method is helpful. Animal inoculation (monkeys) may be required in doubtful cases.

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5. Syphilis, or Lues

Treponema pallidum.—The *Treponema pallidum* (or *Spirochaeta pallida*, Schaudinn) is an extremely delicate, motile, corkscrew-like thread (6–14 turns), at the end of which are extremely minute flagellate extensions; it is present in the lesions of syphilis at all stages. It is best seen

in histological specimens prepared by Levaditi's silver-impregnation method. The methods of demonstrating it by Giemsa's stain, by the india-ink method, and by dark-field illumination have already been referred to. It has been *cultivated* by Noguchi in serum media containing a little sterile rabbit's kidney. It can also be cultivated by the modified method of Schereschowsky.

Fig. 117.—(5, 6 and 7) Treponema pallidum from a Ten-Day-Old Pure Culture in a Horse-Serum-Agar-Tissue Medium. Giemsa Stain, ×1,280. (8 and 9) Long Forms from a Pure Culture. Giemsa Stain, ×1,280. (After H. Noguchi, "Studies from the Rockfeller Inst. for Med. Res.," Reprinted from J. Exp. Med.)

It is pathogenic for human beings, monkeys and rabbits.

Definition of Syphilis.—Syphilis is a chronic infectious disease, due to invasion of the body by the *Treponema pallidum.* It is usually acquired through coitus (GENITAL INFECTION), though sometimes in other ways (EXTRAGENITAL INFECTION of lip, tongue, tonsil, nipple, finger, eyelid, anus, skin abrasion, etc.). Many physicians suffer from syphilis "innocently" acquired (gynecological examination, surgical operations, autopsy infection, etc.). In contradistinction to *acquired syphilis,* there is also a *congenital syphilis,* due either to *fetal infection* from the mother (placental syphilis), or to *germinal infection* (from the father).

(*a*) *Acquired Syphilis*

Four stages are distinguished: (1) a *primary* stage, (2) a *secondary* stage, (3) a *tertiary* stage, and (4) a *metasyphilitic,* or *parasyphilitic,* stage. It is well to remember that the primary, secondary and tertiary stages often merge one into another, so that frequently no sharp line of division can be drawn between them.

Primary Syphilis.—From 3 to 6 weeks after exposure, a pale, firm, painless nodule appears at the site of infection (HUNTERIAN CHANCRE; INITIAL SCLEROSIS). Under treatment, this may disappear without ulceration, but, usually, it breaks down, with the formation of an ulcer, which is also known as a syphilitic chancre, with a *hard, woodlike margin.* It is usually single, in contrast with soft chancre, which is most often multiple, but the initial lesion of syphilis is occasionally multiple. It is most common on the glans penis, but may be situated on the prepuce. Intraurethral chancre may occur; it probably often escapes observation. The chancre usually disappears under mercurial treatment in from 3 to 5 weeks after its full development; under salvarsan treatment, it may disappear much more quickly.

Fig. 118.—Rupia syphilitica. (Med. Service, J. H. H.)

Before the primary lesion has disappeared, the inguinal glands and the retrocervical lymph glands become enlarged and firm. About the same time, the epitrochlear glands may also become palpable. The lymph gland enlargement is always bilateral.

This general lymphadenoid hyperplasia reaches its height in from 7 to 9 weeks.

Secondary Syphilis.—From the 9th to the 12th week, the secondary stage of syphilis is entered upon with the appearance of a macular, rose-colored, or slightly *copper-colored* exanthem (ROSEOLA SYPHILITICA, MACULAR SYPHILID).

This is often preceded by slight prodromal disturbances (fever, nocturnal headache, nocturnal pains in the limbs and bones (DOLORES OSTEOSCOPI). The syphilitic roseola appears first on the skin of the chest, abdomen, or back. It is rarely present on the face, or the extremities, though it is sometimes visible on the uvula, tonsils, and soft palate. Later, whitish areas appear in the mouth (margin of tongue, lips, tonsils, cheeks), the so-called MUCOUS PATCHES and hypertrophic changes in the mucous membranes, especially of the vulva and anus, may give rise to the syphilitic excrescences known as CONDYLOMATA.

In this secondary stage, the patients feel ill (anorexia, progressive anemia, occasionally albuminuria, icterus, and palpable spleen). The hair often falls out (*defluvium capillorum*), and the patients complain of sore throat.

Instead of the macular syphilid, succeeding it, or mixed with it, there may be a papular eruption (PAPULAR SYPHILID). These papules are usually rather small, firm, and of a brownish red or copper color; they are sharply circumscribed and rounded (*lenticular syphilid, large papular syphilid*). On fading, they scale and become indented in the center, leaving a brown pigmented area behind. In more malignant forms of syphilis, the papules are very much smaller, about the size of the head of a pin, brownish red, firm, and distinctly pointed (*small papular syphilid, miliary syphilid, lichen syphiliticus*). The papules undergo slight desquamation, similar to that seen in the larger form. In still other malignant cases, the papules may take the form of quite large nodules that undergo ulceration, simulating that of *gummatous syphilids.*

Instead of a macular, or a papular, syphilid, in the secondary stage, a PUSTULAR SYPHILID or an ULCERATIVE SYPHILID form may be met with. The pustules may be large and surrounded by a red areola. Crusts may form over broken pustules, after which the ulcer may gradually extend at its periphery. In these cases the older central crusts become gradually elevated in oyster-shell-like laminations upon the crusts formed later (RUPIA SYPHILITICA). The superficial form of pustular syphilid affecting especially the scalp and beard is known as IMPETIGO SYPHILITICA. Sometimes small pustules arise on the bases of papular infiltrations, especially

in hairy beards (ACNE SYPHILITICA). Again, in severe cases, the pustular syphilid involves the deeper tissues (ECTHYMA).

Laryngeal catarrh is common in the secondary stage, with hoarseness or aphonia, and laryngeal examination may reveal a papular eruption or mucous patches, or even ulcers of the mucous membrane

Fig. 119.—Scaling Syphilid of Palms. Conditions of Palms Two Weeks After Treatment With "606." See Photograph Before Treatment. (After H. J. Nichols and J. A. Fordyce, "Studies from the Rockefeller Inst. for Med. Res.," Reprinted from J. Am. M. Ass.)

The eruption of the secondary stage often recurs at intervals (*relapses, recidives*). A papular or papulosquamous exanthem on the palms of the hands or soles of the feet is almost pathognomonic of syphilis (= *palmar and plantar syphilitic psoriasis*). An *onychia* or *paronychia syphilitica* is not uncommon in the secondary stage.

Falling out of the hair has already been mentioned. This may be diffuse, or it may occur in patches (*alopecia syphilitica*). The hairs of the beard, axillae, eyebrows, eye-lashes and pubic region may also fall out. Periostitis, occasionally arthritis, peripheral neuritis, neuralgias (trigeminal, intercostal, sciatic), isolated ptosis, diplopia, and optic neuritis are not uncommon. The periostitis often gives rise to NODES on the tibia, ribs or skull.

Unilateral or bilateral iritis, with violent nocturnal pain, is often an early symptom. Sudden deafness due to involvement of the labyrinth may occur.

The lesions of secondary syphilis (at the beginning, and in its periodic exacerbations) are extremely infectious, especially the mucous patches and the condylomata on the genitals or about the anus.

In insufficiently treated cases, the *recurrences* may occur at regular intervals (6 months); more often the intervals are irregular, going on for from 3 to 5 years, to be followed by a *latent period,* before tertiary symptoms manifest themselves.

Fig. 120.—Scaling Syphilid of Palms. Duration of Infection, Three Years; of Palmar Lesions, One Year. May 16, 1910, 0.3 gm. "606." Wassermann Before Treatment, + +; June 10, 1910, Negative; Sept. 1, 1910, Still Negative. See Photograph After Treatment. (After H. J. Nichols and J. A. Fordyce, "Studies from the Rockfeller Inst. for Med. Res., Reprinted from J. Am. M. Ass.)

Two additional constitutional symptoms of the secondary stage deserve especial mention:

1. The FEVER may be extremely variable in character. Thus it may be slight and of brief duration. Sometimes it is continuous, simulating that seen in the second week of typhoid fever. Sometimes it is remittent over long periods of time, leading to a diagnosis of tuberculosis. Or, again, it may be paroxysmal and intermittent, simulating the pyrexia of malarial fever.

Fig. 121.—Alopecia Syphilitica. (After Marschalko, from Török's Article in E. Riecke's Lehrbuch, published by G. Fischer, Jena.)

2. The ANEMIA is often pronounced. It is of the secondary type (low color index). A hematogenous jaundice, due to rapid destruction of erythrocytes, may develop. There is rarely a leukocytosis, but a relative increase in the mononuclear cells is the rule.

Tertiary Stage.—The characteristic lesion in this stage is the GUMMA (aggregations of small mononuclear cells which tend to break down from coagulation necrosis). The ulceration resulting heals with difficulty and gives rise to dense scars, which cause marked deformity of parts affected. The gummata may vary in size from that of a pin's head to that of a child's head, or larger. They are very common in the skin, periosteum and bones, less common in the muscles.

In some instances, the viscera (liver, lung, spleen, intestine, kidney, heart) are predominantly involved (VISCERAL SYPHILIS). Gumma of the brain may give rise to symptoms and signs of brain tumor. A gummatous arteritis of the brain may cause hemiplegia, or aphasia. Gummatous arteritis in the spinal cord is a frequent cause of paraplegia. *Gummata of bone* are most often met with in the skull, clavicle, sternum and tibia. The bones of the nose may break down (*saddle-nose*); the bony atrophy is often followed by ozena. Perforation of the nasal septum is not uncommon. Perforation of the palate may also occur; white scars on the hard or soft palate are suspicious of preëxisting luetic lesion. In the tongue, a gumma may simulate carcinoma or actinomycosis.

Gumma of the liver is of great practical importance, sometimes being mistaken for carcinoma. Syphilitic cirrhosis is multilobular.

In the intestine, syphilitic ulcers often cause strictures with stenosis, especially in the rectum. Gummatous processes in the esophagus and trachea, also, sometimes give rise to strictures.

Luetic arthritis is rather rare, being much less common than luetic periostitis. A gummatous mesaortitis is the commonest cause of AORTIC ANEURISM and of ISOLATED AORTIC INSUFFICIENCY. Amyloid disease is not uncommon.

Paraluetic Stage.—Ten, fifteen, or more, years after infection, symptoms of *parasyphilis* may develop, giving rise to (1) the clinical picture known as general paresis or DEMENTIA PARALYTICA, when the *Treponema pallidum* invades the cerebral cortex itself, or (2) the picture of TABES DORSALIS (locomotor ataxia) when the spinal meninges and roots of the sensory nerves are involved, leading to degeneration of the posterior funiculi of the spinal cord. (See Part XII.)

Diagnosis.—No reliance should be placed upon the anamnesis, unless it is positive. The nature, site and appearance of the lesions are often characteristic. In primary and secondary lesions, the presence of the *Treponema pallidum* may be demonstrable. (See Methods.)

In *all stages of syphilis*, except in the early stage of the hard chancre, and during and for two weeks after antiluetic treatment, the WASSERMANN REACTION (q. v.) is positive in a large percentage of the cases.

In *lues cerebrospinalis*, the cell count of the cerebrospinal fluid, the increase in globulin content, and the positive Wassermann reaction in this fluid, aid in diagnosis.

In the *paraluetic diseases,* the neurological phenomena (q. v.), the lumbar puncture, and the Wassermann reaction make diagnosis, as a rule, easy.

Care should be taken not to confuse tertiary luetic lesions of the bones and skin with (1) *tuberculosis* or (2) *sporotrichosis* (q. v.).

(*b*) *Congenital Syphilis*

The fetus may be infected through the placenta. In such cases the mother is infected (positive Wassermann reaction), though the disease may be entirely latent in her as far as symptoms are concerned. According to COLLES' LAW, a child suffering from congenital syphilis may infect a healthy nurse, but cannot infect its own mother, even though she suckle it.

Fig. 122.—Twins with Hereditary Syphilis. R = Diffuse Infiltration of the Skin, Very Marked, Especially on Hands, Arms and Feet. Syphilitic Crusts About the Mouth and Chin. L = Circumscribed Pustular Syphilide on the Face, Especially the Forehead. Rhagades at the Edges of the Lips. (After Pfaundler, in E. Feer's "Lehrb. d. Kinderheilkunde," published by G. Fischer, Jena.)

The reason is that the mother is already infected. Again, if a woman, suffering from lues, bear a child that shows no symptoms of syphilis, the child does not contract the disease if suckled by its mother (PROFETA'S LAW). This may be due to the transference of a passive immunity to the child *in utero,* but is more likely due to the fact that the child is already the bearer of latent infection (Diday).

Symptoms.—Many of the children are still-born, or die soon after birth (feeble development, pemphigus neonatorum syphiliticus).

Children may be born apparently healthy, and in one or two months develop snuffles (*syphilitic rhinitis*), fissures and scabs at the angles of the mouth (*rhagades*), syphilitic onychia, and enlargement of the spleen and lymph glands. Violent, unmotived crying, during the early months of life, should make one suspect the possibility of congenital syphilis.

In childhood, symptoms often reappear at the period of the second dentition, or at puberty. Various *dystrophic signs* are more or less characteristic; among these are infantilism, saddle-nose, scars of rhagades, Hutchinsonian teeth (the upper permanent central incisors being peg-shaped and crescentically notched at the cutting edge), interstitial keratitis, bosses on the frontal bones, chronic gummatous periostitis.

Fig. 123.—Hutchinson's Teeth in Hereditary Lines. Note the Concave Defect in the Edges of the Medial Upper Incisors. (From Buschke's Article in Eulenburg, Kolle and Weintrand's "Lehrb. d. klin. Untersuchungsmethoden," published by Urban & Schwarzenberg, Berlin.)

A child may be free from syphilis in its early years, and later on present definite symptoms (SYPHILIS HEREDITARIA TARDA). Whether or not the disease can be transmitted to the third generation, is still in dispute.

Juvenile tabes and juvenile paresis occasionally occur.

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6. Yaws or Frambesia

Definition.—A disease of tropical countries characterized by papular, tubercular and ulcerative skin lesions, and manifesting itself in a primary, secondary and tertiary stage analogous to those of syphilis. The causative organism is the *Treponema pertenue.*

Etiology.—By many authorities yaws was confused with syphilis until Castellani in 1905 demonstrated the presence in the skin lesions, lymph nodes, and

[illegible] of the *Treponema pertenue*. This discovery has since been abundantly con[illegible]. The distinction between yaws and syphilis is likewise supported by th[illegible] that there have been many instances of the development of yaws naturall[illegible] and by inoculation in those affected with syphilis.

Symptoms.—After a *period of incubation* of from 2 to 5 weeks the *initial lesio*[illegible] appears at the point of inoculation as a small papule. The overlying skin soo[illegible] ulcerates, exposing a fungoid yellowish-red base from which seropurulent flui[illegible] exudes. This mass of fungoid granulations may attain 1 to 2 inches in diamete[illegible] The primary lesion is usually extragenital.

The secondary stage sets in in from six weeks to three months after the appear[illegible]ance of the initial lesion. There is a generalized eruption of papules entirel[illegible] similar to the primary lesion. The face, neck, perineum and the extremities ar[illegible] especially affected. Frequently the eruption is accompanied by marked itching[illegible] The character of the lesions is very uniform in contrast to the pleomorphism tha[illegible] is common in syphilis. The onset of the secondary stage is usually attended wit[illegible] fever, headache and joint pains. There may be successive eruptions of yaw[illegible] tubercles prolonging the secondary stage for two to three years. More usuall[illegible] it lasts only three or four months.

Certain cases of yaws exhibit a *tertiary stage* of which the characteristic lesion[illegible] are gummatous nodules and deep ulcerations (Castellani). It is possible that th[illegible] condition known as *gangosa* (q. v.) is simply tertiary yaws of the nose and palat[illegible] There appears to be no tendency in tertiary yaws to involvement of the viscera o[illegible] of the central nervous system.

Prognosis.—The death-rate is very low—approximately ½ of 1 per cent. Re[illegible]covery does not yield complete immunity; reinfection may occur.

Diagnosis.—The juice from yaws tubercles should be stained by the India in[illegible] method or with Giemsa's stain. The *Treponema pertenue* closely resembles the *Tre*[illegible]*ponema pallidum*; it is, however, somewhat thicker, the spirals are less regularl[illegible] formed, and the ends more blunt. In sections of the lesions, stained by Levaditi[illegible] method, the treponema is found in the epidermal layer instead of in the coriun[illegible] as in syphilis.

Clinically the extragenital site of the primary lesion of yaws; the similarity o[illegible] the primary and secondary lesions; the uniformity in the appearance of these la[illegible]ter; the rarity of involvement of mucous membranes in yaws help to differentiat[illegible] from syphilis. On the other hand salvarsan is more specific for yaws than fo[illegible] syphilis, and the Wassermann reaction is more frequently positive in yaws.

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7. Granuloma venereum

(Ulcerating Granuloma)

Definition.—A chronic superficial ulceration in the region of the genitals occur[illegible] [illegible] chiefly in tropical countries. A few cases have been reported in the Unite[illegible] States.

Etiology.—The causative organism has not been definitely ascertained. It i[illegible] probably a spirochete resembling *Treponema pallidum* (Wise).

The disease is transmitted by sexual intercourse. It is somewhat more commo[illegible] in women.

Symptoms.—The disease first manifests itself as a small painless papule or nodule on the penis, the labia, or the perineum. This lesion ulcerates and the ulceration then spreads by continuity to the groins and the inner surface of the thighs. The margin of the ulcer is usually clean-cut and steep. The base of the ulcer is often covered with a gray membrane. The granulations bleed easily. The discharge is usually profuse and offensive. The process is very chronic. Healing occurs with scar-tissue formation. The ulceration may involve the vagina, and rectovaginal fistulae often result. The lymph glands are not affected. The process is comparatively painless. The general health is impaired only when the area of the ulceration is extensive.

Diagnosis.—The disease must be differentiated (1) from *syphilis* (secondary symptoms; enlarged lymph nodes; Wassermann positive, response to specific treatment) and (2) from *tuberculosis* (histology of excised material).

8. Gangosa

Definition.—A destructive ulceration of the palate and nasal passages occurring in tropical countries.

Etiology.—Gangosa is usually regarded as a tertiary manifestation of either yaws or syphilis. The absence of other forms of syphilis in Guam, where gangosa is prevalent, speaks strongly against the latter supposition. In 315 cases of gangosa Kerr found only 18 in whom scars or a history of yaws were lacking.

Symptoms.—The disease usually begins with ulceration of the palate, which very rapidly spreads upward destroying the bone and cartilage forming the tip of the nose. The nasal ducts are frequently involved with consequent loss of one or both eyes. The active process may subside in one or two years, leaving marked deformations. Ozena is a common accompaniment.

Diagnosis.—Syphilis is hard to rule out, since entirely similar lesions may occur in the malignant form of that disease. A large percentage of cases of gangosa give a positive Wassermann test. Salvarsan is curative. The possibility that the disease is a special form of either syphilis or yaws should be kept in mind.

9. Verruga peruviana

Definition.—A tropical disease confined to certain valleys of Peru, apparently an infectious granuloma.

Symptoms.—It is characterized by an eruption of vesicles and papules over the extremities and face. Later on, subcutaneous nodules appear, which may reach 3-4 cm. in diameter. The skin over them frequently ulcerates and red fungous masses result. Verruga nodules have also been found in the internal organs. After several weeks or months the eruption disappears, but relapses are common.

As a result of the work of R. P. Strong, E. E. Tyzzer, A. W. Sellards and C. T. Brues of the Expedition to South America from the Harvard School of Tropical Medicine, verruga peruviana has been sharply separated from Oroya fever, which had formerly been considered to constitute the febrile stage of verruga. The virus of verruga peruviana is transmissible to monkeys, but has not been shown to be filtrable.

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10. Oroya Fever

(*La Maladie de Carrion*)

Barton in 1909 and later Strong have reported as the etiological agent in this fever a parasite of the red-blood corpuscles sufficiently distinct from the other hematozoa previously described to permit it to be placed in a new genus. The name *Bartonia bacilliformis* has been proposed for this organism. The disease is characterized by high fever, a rapid and pernicious form of anemia, extreme prostration and death. In Peru, where it is common, it is frequently combined with verruga peruviana. In 1885 a young medical student, Daniel Carrion, in an attempt to settle the question of the identity of the two diseases, allowed himself to be inoculated with the blood of a patient with verruga peruviana. Within thirty-nine days he succumbed to an apparently typical attack of Oroya fever. The confusion of identity caused by this outcome may be compared to that following the famous experiment of John Hunter with syphilis and gonorrhea.

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C. Diseases Due to Pathogenic Sporozoa

The *coccidia* (coccidiosis), and the *sarcosporidia* (Miescher's tubes in striped muscle), are, in this country, unimportant for human pathology; as *hemosporidia*, the malarial parasites were formerly included under pathogenic sporozoa. They have already been considered, above, in their new position, under the flagellata.

III. DISEASES DUE TO FILTRABLE OR "ULTRAMICROSCOPIC" VIRUSES

Filtrable Viruses.—A number of diseases are due to forms of virus that will pass through fine PORCELAIN FILTERS. The virus is therefore believed to be smaller than bacteria. The pores of the filter are, it is true, larger than bacteria, but bacteria do not get through on account of the tortuous passage. *Berkefeld filters*, made of diatomaceous earth, are more porous than *Pasteur-Chamberland* filters, made of unglazed porcelain kaolin.

Studies of these viruses should be undertaken by the newer methods of studying colloid particles of different sizes. Among these may be mentioned (1) the observation of Tyndall's phenomenon (illuminated pyramid, on lateral observation, in a fluid, when a small bundle of light rays is projected through the fluid) by the ULTRAMICROSCOPE, of which there are two main types: (a) the *slit*

ultramicroscope of Siedentopf and Zsigmondy, and (b) the *cardioid-ultramicroscope* of Siedentopf; and (2) the method of "ULTRAFILTRATION" OF BECHOLD, in which the pores of the filter are covered with gels of different concentration, each concentration permitting colloid particles of definite size to pass through but preventing the passage of particles of larger size. So delicately do these filters work, that it is possible by them to separate diphtheria toxin from toxon (Bechold), and to separate the colloid particles of boiled milk from those of raw milk (Grosser).

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A. Disease Due to Pasteur's Virus

Virus of Rabies.—The nature of the virus is unknown, unless it be the organism recently described by Noguchi (see below); but it is present in the saliva of animals suffering from *rabies,* and is concentrated in the tissues of their nervous systems. To cause disease, it must be inoculated into the tissues; swallowed, it is harmless. All mammals are susceptible, but the dog seems to be the animal that keeps the disease going. Possibly healthy dogs may be chronic carriers.

1. Rabies

(*Hydrophobia, Lyssa*)

Definition.—An acute, fatal infection (after a long incubation period), municated to man, usually by a rabid dog, sometimes by other infected unk, wolf, horse, cat, etc.).

Period; Immunity; Virus.—In this disease, which is always ptoms have developed, the *incubation period* is longer,

and more variable, than in any other acute infection. It varies from 14 days to a year or more, the average, in man, being 40 days.

Active immunity can be produced in man by PASTEUR'S PREVENTIVE INOCULATION in about 15 days. Since this is a much shorter period than the incubation period, *prompt action will nearly always, though not always, prevent the disease*, though in bites upon the face, the incubation period is shorter, and rabies sometimes develops, despite preventive inoculation.

The virus appears in the saliva of the dog 3 to 8 days before the animal shows symptoms. A dog kept under surveillance for 10 days after biting a human being, or another animal, is probably free from rabies if no symptoms develop during that period.

A skin lesion is necessary for infection in human beings, and the virus, like the tetanus toxin, appears to travel to the central nervous system along the nerve trunks. Even when a person has been bitten by a mad dog, and left untreated, rabies does not necessarily develop. Probably not over 10 to 15 per cent of people so bitten would develop the disease (Paltauf).

The virus is killed by prolonged drying, by sunlight, and, quickly, by heat and by disinfectant solutions. It is not injured by extreme cold (liquid air) or by putrefaction. Glycerin preserves it, though it kills bacteria.

Recently (1913) Noguchi reports that he has cultivated the virus of rabies from the nervous system of infected rabbits, killed before the disease terminated naturally. He places the material in ascites fluid, along with a small piece of sterile rabbit's kidney, just as in his method of cultivation of the Treponema pallidum. After incubation, he found in some of the tubes, on microscopic examination, granular chromatic corpuscles of variable size. Some were on the limits of visibility; others were as large as 0.2-0.3 μ. He also saw groups of minute pleomorphic chromatoid particles, measuring 0.2-0.4 μ broad by 0.4-0.5 μ long. In Giemsa's stain, these take a red or a bluish color. He was able to grow them for several generations in the medium mentioned. Sometimes, he found in the cultures larger corpuscles varying in size from 1 to 12 μ; the inner bodies of these stained dark blue or violet, the outer part azure, and the membrane reddish; some of these he asserts are identical with Negri bodies. Injected into rabbits, guinea-pigs, and dogs, these minute corpuscles give rise to typical rabies. Should this finding be confirmed, the microorganism might well be called *Pasteuria negrii* (*Noguchi*).

Symptoms.—In from 2 weeks to 6 months after the bite, the wound begins to redden, and to become painful, and the bitten person becomes depressed and restless, and complains of headache and of sleeplessness (*prodromal stage*, or *stadium melancholicum*). Two to 4 days later, the stage of excitement (*stadium hydrophobicum*) begins; tonic spasms appear in the muscles of the pharynx and of the larynx. The respiratory muscles also become involved; the patient has difficulty in breathing, and

Fig. 3.—Trypanosoma gambiense. (After Chatard & Guthrie, 1914, Case Observed in Baltimore.)

Fig. 4.—Negri Bodies. (After L. Mohr u. R. Staehelin, "Handb. d. inner. Med.," published by J. Springer, Berlin.)

feels as though he were suffocating. There may be salivation and severe thirst, with inability to swallow, attempts at swallowing causing pharyngeal spasm so that the patient fears to touch water (*hydrophobia*). The patient becomes restless, jumps about in an excited way, cries out, strikes at people and objects about him; in other words, he is a "raving maniac." This stage lasts 1½-3 days (v. Koranyi). He then enters upon the last, or *paralytic stage* (*stadium paralyticum*); there is rapidly developing weakness, and paralysis of various muscle groups (face, tongue, eye-muscles, extremities). The temperature rises, and death occurs within 2 to 18 hours after the paralytic stage sets in. In the so-called "QUIET FORM" the stage of excitement does not occur, the prodromal stage going directly over into the paralytic stage. Recently, ABORTIVE CASES have begun to be recognized (Remlinger, Simon).

Diagnosis.—It is most important, after a dog-bite, to determine whether or not the animal is really infected. It should be caught, immediately, alive if possible. Formerly it was advised that it be kept under surveillance for a few days. If one is fairly sure that the dog is not mad, this may be permissible; if there is strong suspicion, the dog should be killed at once, the brain should be aseptically removed, and the medulla oblongata placed in pure glycerin and sent to a *bacteriological laboratory* or to a *Pasteur Institute,* for the experimental inoculation of rabbits; further, a piece of the horn of Ammon and a piece of the spinal cord and of a posterior root ganglion should be fixed in formalin and sent to a *histological laboratory* for examination (1) for NEGRI BODIES in Ammon's horn; (2) for the NODULES RABIQUES OF BABES (collections of small pericellular foci of mononuclear cells around the nerve cells of the spinal cord), and (3) for THE LESION OF VAN GEHUCHTEN AND NELIS, specific changes, revealed by Nissl's methods, in the nerve cells of the sensory and sympathetic ganglia.

For INOCULATING THE RABBITS, an emulsion of the fresh or of the glycerin-preserved medulla or spinal cord, is injected beneath the dura, after trephining; or intracerebral injection may be employed. If the virus be present, the animal injected will show signs of rabies, in most cases, before the 21st day. At least two rabbits should be inoculated. In case the cord is not aseptic, and especially if putrefaction has begun, it is better to make intramuscular rather than subdural injections; further, the material may be rubbed up in 1 per cent carbolic acid solution and left in the ice-box for 24 hours before injection (Marx), or the brain may be laid in pure glycerin for 48 hours before injection (Nicolle), to kill any bacteria present.

In EXAMINING FOR THE NEGRI BODIES, which can be found in 90 to 95 per cent of all infected animals, a piece of Ammon's horn is fixed in formalin, quickly hardened in alcohol, and imbedded in celloidin or paraffin, sectioned, and stained with Wilson's stain, or with eosin methylene blue (Plate VIII, Fig. 4), or by van Giessen's method.

A quicker method still is to make smears by crushing a small portion of Ammon's horn between two slides, fixing, and proceeding to stain by the Mallory eosin blue method as follows (Williams and Lowden):

1. Treat with Zenker's solution for 15 minutes.
2. Wash in tepid water.
3. Place in 95 per cent alcohol tinged with iodin.
4. Dehydrate 5 minutes in absolute alcohol.
5. Stain 5 minutes in aqueous solution of eosin (Grubler, W. G.) 5-10 per cent.
6. Stain 2-3 minutes in Unna's polychrome methylene blue.
7. Wash in water.
8. Differentiate in 95 per cent alcohol, blot, dry, mount, and examine with immersion lens.

Lentz's method is as follows:

1. Imbed in paraffin by the quick method of Henke-Zeller:
   (a) 4 per cent formalin-fixation of piece ½ cm. thick for 15 min.
   (b) Pure acetone for ½-1½ hours, changing 2-3 times.
   (c) Xylol 15 minutes.
   (d) Paraffins (several) ½-1½ hours.
2. Stain section 1 minute in
   Eosin extra a. B. (Hoechst).....0.5 g.
   Alcohol (60 per cent).....100.0 c.c.
3. Wash in water.
4. Stain 1 minute in Loeffler's methylene blue.
5. Wash. Dry partially with filter paper.
6. Differentiate in:
   Absolute alcohol .....60 c.c.
   NaOH (1 per cent).....10 drops
   Leave in, until the color is pale red.
7. Differentiate further in:
   Absolute alcohol .....60 c.c.
   Acetic acid (50 per cent).....2 drops
   Leave in, until the ganglion cells are pale blue.
8. Dehydrate quickly in absolute alcohol; clear in xylol; mount in neutral balsam.

The Negri bodies are carmine red; the inner bodies are blue; the red blood corpuscles, brick red; cell-nuclei, dark blue; protoplasm, pale blue.

The *Negri bodies* are round or oval structures, situated inside the ganglion cells. They possess a membranous, capsulelike structure, and, in the interior, show a differentiation, due probably to vacuoles (?). According to Negri, they are protozoa (*Neuroryctes hydrophobiæ*), and are the cause of the disease. They are exclusively, and almost constantly, present in rabies, but they cannot be found in some material that certainly contains the virus (saliva, salivary glands), and they are present, in very small numbers, in the spinal cord. Moreover, even in Ammon's horn, where they are abundant late- emonstrated in the incubation

period, though this tissue at the time is extremely infectious. The Negri bodies do not pass through a Berkefeld filter, but a virus capable of producing rabies does pass through.

In rabbits killed by *virus fixe,* Lentz finds peculiar structures *between,* not *in,* the cells of Ammon's horn; they resemble Negri bodies, but are not identical with them. These "passage-virus corpuscles" are not present in rabbits killed by "street virus."

On examining for the lesions of van Gehuchten and Nelis, it is best to section the ganglion on the vagus nerve or the Gasserian ganglion. If the lesion be present, the endothelial cells surrounding the ganglion cells will be found proliferated, the nerve cells being pushed aside and many of them destroyed.

If a person has not been bitten, but simply licked on the hands or face by a mad dog, there is probably no danger, unless there have been fissures or abrasions on the skin at the time. Where any doubt exists, the preventive treatment should be taken.

Pasteur's Treatment for the Prevention of Rabies (1883).—A great boon was conferred upon mankind by Pasteur's application of the principle of producing an active immunity by means of an attenuated virus, in the prevention of rabies. By passing the "street virus" (obtained from a dog naturally infected) through a series of rabbits, the virulence is increased, until the so-called "fixed virus" (of constant potency) is obtained. This fixed virus causes rabies in rabbits by the 6th day, killing them on the 9th or 10th day, but, strangely enough, has largely lost its virulence for dogs, and is probably entirely avirulent for man (Proescher).

The spinal cord of a rabbit, chloroformed on the ninth day after inoculation with fixed virus, is removed, and desiccated for 14 days. A segment of the cord, cut off each day, is kept in pure glycerin. Glycerin emulsions are made of the different segments. Two doses of the most attenuated virus are given on the 1st day, and on each successive day a dose of progressively less attenuated virus is given until, by the 18th day, a virus made from the cord that has been dried only 3 days is given.

The treatment is best carried out at regularly established **Pasteur Institutes,** but emulsions of the cord in glycerin can now be sent to a distance and the treatment can be carried out at home.

There is no longer any doubt about the value of this prophylactic inoculation.

Neglect to begin the treatment early enough is often followed by the most disastrous results. In Chicago, I saw 3 cases of human rabies. Half an hour after I had shown one man, with beginning symptoms, in the clinic at Rush Medical College, I was summoned to his room in the Presbyterian Hospital to find him violently insane, threatening all who came *ar him.* He had to be overpowered. One plucky interne rushed in *i a* blanket in front of him, followed by a group of men, and together

they secured the patient; he had to be kept under chloroform for a few hours until the exitus!

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B. Disease Due to Reed, Carroll and Agramonte's Virus

Virus of Yellow Fever.—This virus, studied by Reed, Carroll, Lazear and Agramonte, is the cause of yellow fever. The virus is present in the blood during the first 3 days of the fever only. If the infected human being be bitten, at this time, by a particular variety of mosquito (*Stegomyia calopus fasciata*), the virus undergoes some form of development within the body of the mosquito, and, after about 2 weeks, if the same mosquito bite a healthy human being, the latter may become infected. The findings of the United States Army Commission (Walter Reed and his colleagues) have been confirmed by the French Expedition in Brazil (Marchoux and Salimbeni).

It was shown that the blood of a patient in the first three days of the disease would, if injected subcutaneously, produce the disease in a susceptible person. Cutaneous vaccination with infected serum is without result. The virus in the blood will pass through a Berkefeld filter. It has not as yet been cultivated.

1. Yellow Fever

Definition.—Yellow fever is an acute and severe infectious disease, transmitted by infected mosquitoes. It was formerly very prevalent in Central America and the West Indies, and sometimes invades the Southern United States. It is due to the filtrable virus of Reed, Carroll and Agramonte.

Epidemiology.—The disease was first described in Guadaloupe in 1635

and has been endemic since then on the islands and on the coasts of the Gulf of Mexico and the Caribbean Sea and on the West Coast of Africa. The United States of America, Spain and Brazil have suffered from severe epidemics. That in Philadelphia in 1793 was interestingly dealt with in the medical writings of that day. The theory of transmission by fomites was greatly stressed but the observation that the larger number of cases developed in certain streets near the wharves led some authors to attribute importance to "miasmatic vapors" from the water. We now know that the *Stegomyia calopus* is preëminently "a house mosquito and a town mosquito" breeding in the water of cisterns, roof gutters, old tin-cans, etc., and rarely traveling further than 75 feet from the house in which it has been feeding. The screening of all cases of yellow fever, and the draining, or oiling, of all standing water to eliminate the *Stegomyia*, have freed Havana, Porto Rico, and the Panama Canal Zone of this dread disease.

Symptoms.—The incubation period is 3-5-13 days. The onset is sudden with chill, fever, tachycardia, severe pains in the small of the back and in the extremities, congestion of the face and of the conjunctivae, and sore throat. There is marked tenderness in the epigastrium on palpation, and vomiting. The patients give off a "butcher-shop odor." The definite icterus, which appears on the third day, is important for diagnosis. In from 2 to 4 days, there is a sudden fall of the temperature to normal, often with collapse and exitus; in non-lethal cases, defervescence is usually by lysis. The remission, in other cases, lasts only a few hours, and is generally followed by a secondary fever of 1 to 3 days duration; if the patient live, gastric, cardiac, renal and hepatic symptoms appear. Albuminuria and cylindruria are found more constantly and earlier in yellow fever than in any other infectious disease. Among other phenomena often observed are hematemesis (black vomit), enterorrhagia, and cardiac insufficiency. A frequent finding is the presence of an increasingly marked bradycardia with increasing febrile reaction. The patients generally appear bright mentally; occasionally deliria develop. The mortality is variable in different epidemics (15 to 90 per cent.). Even severe cases may recover. Relapses are common. In times of epidemic mild and abortive cases are often met with, especially in children. One attack gives complete immunity.

Diagnosis.—This may be very difficult, especially at the beginning of an epidemic. The disease must be differentiated: (1) from malaria (parasites in stained smears or in fresh blood, absence of early jaundice, larger spleen); (2) from relapsing fever (spirochaetes); (3) from phosphorus poisoning (anamnesis); (4) from acute yellow atrophy of the liver (convulsions, delirium); (5) from dengue (absence of flushed facies of yellow fever, of albuminuria and of the late bradycardia (Faget's sign in yellow fever), and of the early jaundice).

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C. Disease Due to Ashburn and Craig's Virus

Virus of Dengue Fever.—This filtrable virus, as shown by Ashburn and Craig, who studied the disease in the Philippines, can be transmitted by mosquitoes (*Culex fatigans*), though no especial cycle seems to be gone through by the parasite in the body of the mosquito. Contact infection may occur, but is probably rare.

1. Dengue Fever

Break-Bone Fever, Dandy Fever

Definition.—An acute, infectious, non-fatal, tropical fever, accompanied by severe pains in the bones, joints and muscles, and by rashes at the beginning and at the end of the disease; due to a filtrable virus, and occurring, usually in the hot weather, in sharply circumscribed epidemics, or occasionally, sporadically.

Symptoms.—After an incubation period of from 3 to 5 days, there is sudden fever (105°-107° F.), with headache, chilly sensations, muscular and articular pains, and a skin exanthem (initial erythema). The joint and bone pains are excruciating and may persist for many weeks.

The fever is maximal by the 3rd or 4th day; then there is apyrexia for from 2 to 4 days, followed by a return of the fever and the pains. The disease is associated with a leukopenia. The non-itching rash, which on the 4th or 5th day usually appears on the palms and backs of the hands, forearms, chest and back, consists of small red papules and macules, not unlike the eruption of measles. There is generally lymphglandular enlargement, which may persist long after recovery. On the 6th or the 7th day, the temperature falls by crisis, and the disease is practically over, though the skin eruption may disappear but slowly. In convalescence, prostration of unusual grade may be present. The immunity yielded by a single attack does not last long (1 year).

Diagnosis.—Easy enough to recognize in epidemics, dengue may be difficult to diagnosticate in the first few cases. In the differential diagnosis we have to distinguish it (1) from *yellow fever* (q. v.); and (2) from *influenza,* in which the pains in the muscles and joints are less severe, and the respiratory catarrhal symptoms are more marked; herpes is more common, and the *B. influenzæ* is present in the sputum.

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D. Diseases Due to Flexner and Noguchi's Filtrable and Cultivable Virus (Flexneria noguchii)

Flexner and Noguchi's Virus of the Heine-Medin Disease.—The virus of acute poliomyelitis has been shown by Flexner to belong to the class of filtrable viruses. Noguchi and Flexner have recently cultivated it (see below), and though supposed to be ultramicroscopic, because filtrable, it is visible in stained preparations of cultures and of infected tissue, being a small sub-coccoid body (0.2 μ), much smaller than any known bacterium.

1. Heine-Medin Disease

Infantile Paralysis, Acute Anterior Poliomyelitis

Definition.—An acute, infectious disease occurring both in epidemics and sporadically, due to the filtrable and cultivable virus *Flexneria noguchii* and involving different parts of the nervous system, often localizing especially in the anterior horns of the gray matter of the spinal cord

(poliomyelitis anterior), but also localizing in the cerebrum, in the medulla oblongata, in the cerebellum, and in the meninges, to a variable extent in different cases (cerebral, bulbar, cerebellar, polyneuritic, meningeal, and abortive types).

Historical.—Knowledge of the disease has been much increased since the early clinical studies of Heine, of Cannstadt (1840), who called it "infantile spinal paralysis." Strümpell later studied forms of *cerebral* paralysis which he thought must have the same etiology as Heine's disease. A great advance came through the studies of the Swedish observer Medin (1890), who, in an epidemic, recognized that while *spinal* paralysis predominates, there occur also *cerebral*, *bulbar*, *polyneuritic*, and peculiar *ataxic* forms of the disease evidently due to the same virus. The careful studies of Wickmann (1905-6) in Sweden enlarged our views of the Heine-Medin disease still further, as he demonstrated the existence also of a *meningitic* form, of a form following the course of *Landry's paralysis*, and, above all, of an *abortive* form. Wickmann must be regarded as the founder of the *epidemiology* of the disease, since through his discovery of abortive types, the explanation of the transmission from case to case begins to be better understood. The study of the *pathological anatomy* of the disease began with Charcot's observations on the anterior horns and has made steady progress since, being contributed to in this country especially by S. Flexner and his colleagues. In 1908 began the very important *experimental* studies of the disease; in that year, Landsteiner and Popper successfully infected monkeys with the Heine-Medin disease by intraperitoneal injection. In 1909, Flexner and Lewis showed that the disease could be kept going in a series of monkeys, by passing it from monkey to monkey, a fact also demonstrated by others (Leiner and v. Wiesner; Römer; Landsteiner and Levaditi), the disease being most easily transmitted by intracerebral injections, especially after a "passage virus" has been obtained (Römer, Flexner). Other animals are not susceptible.

These findings gave an enormous spur to the study of the *etiology* of the disease. It was soon shown that the juices of the nervous system of an infected animal, when filtered through a porcelain, or other filter, are still capable of infecting monkeys (Flexner and Lewis, Landsteiner and Levaditi); in other words, the disease is due to a so-called *filtrable virus*. The virus is very resistant to glycerin; it retains its virulence in diluted glycerin 142 days (Römer); even in 33 per cent glycerin it may be fully virulent after 202 days (Levaditi, Landsteiner and Pastia). In this respect it resembles the virus of rabies and that of vaccinia. It stands cold well, retaining its virulence when kept frozen for at least 11 days. It is enfeebled by a temperature of 45° C. and is killed after heating for half an hour at 55° C. It is not killed by drying. It can live for some time in sterile water or sterile milk, apparently without multiplication. Recently, Flexner and Noguchi (1913) have grown the virus outside the body, in

ascites-fluid agar containing a piece of normal rabbit's kidney, the whole culture being covered with a layer of paraffin. The anaërobic colonies appear as a turbidity in the medium. On staining with one of the Romanowsky stains minute violet rounded-oval bodies, singly, in pairs, and in chains, can be seen; they are Gram-positive; examined fresh in the dark field, they are non-motile. The average diameter is 0.2 μ. Monkeys inoculated with the virus develop the disease, even when the virus used has been grown for 20 generations on an artificial medium. The minute parasite is visible in sections of the affected nervous tissue, on careful search. Since the parasite of kala-azar has been named *Leishmania donovani,* might we not do well to give to this virus of the Heine-Medin disease the name *Flexneria noguchii?* Now that one filtrable virus has been cultivated *in vitro,* and has become visible on microscopic examination, there is reason to hope that we are on the threshold of a new era as regards our knowledge of diseases due to filtrable viruses. (See also Noguchi's studies of rabies-virus.)

Transmission by insects has been suspected. That the virus may be transmitted from one monkey to another through the bite of the stable-fly (*Stomoxys calcitrans*) has been demonstrated by Rosenau.

The prevalence of the disease has been increased all over Europe and America in recent years. The virus is concentrated in the central nervous system (spinal cord) of infected persons and animals. One one-hundredth of 1 c.c. of an emulsion of spinal cord will infect a monkey. In infected persons and animals, the virus is present in (1) the nervous tissues, (2) the mesenteric glands (Flexner and Lewis), (3) in the tonsils and throat (Flexner and Clark, Landsteiner, Levaditi and Pastia); in one instance, it has been possible to demonstrate it in washings of the mouth of the healthy parents of a poliomyelitic child (Flexner, Clark and Fraser). It may also be present in the feces. It is probable that the virus can be carried for months, or perhaps for years, in a virulent state, in the throat and tonsils. Such *virus carriers* must be a great menace to a community. The blood and cerebrospinal fluid as a rule are free from the virus. The virus appears to travel along the perineural lymph channels into the central nervous system, rather than by way of the blood vessels; here, again, it is like rabies. The *elective affinities* of the virus for the nervous system on the one hand and for the lymphatic system on the other are striking features of the Heine-Medin disease.

Immunity.—A high degree of immunity is yielded by a single attack. Areas in which the disease is epidemic in one year may be singularly free from it during epidemics of the next succeeding years. The blood serum of a person who has had the disease will neutralize fatal doses of the virus (Anderson and Frost; Flexner and Lewis; Landsteiner and Levaditi; Netter and Levaditi; Römer); the principle can be used to corroborate the clinical diagnosis (*q. v.*) in abortive cases. Monkeys that have

had the disease and have recovered, with residual paralysis, cannot be experimentally re-infected (Römer). Attempts to immunize by applying the method used by Pasteur in rabies are not devoid of danger, since drying the spinal cord does not always attenuate the virus. More can be expected from attenuation by heating to 50° C. (Römer; Landsteiner; Levaditi and Pastia), or by treating the virus with 1 to 1½ per cent carbolic acid for 6 days (Kraus). The most hopeful experiments in the direction of a prophylactic immunization for man would seem to be by serovaccination (Römer).

Human beings are probably infected by way of the upper respiratory passages (nose and throat), possibly also by way of the digestive tract. The possibility of infection by insect bites has been referred to above.

Occurrence in Epidemics.—Large epidemics apparently did not occur until about 30 years ago, though sporadic cases of the disease have been known for over a century. Up to 1907, the large epidemics were confined to Scandinavian countries; since 1907, large epidemics have occurred in most civilized countries (United States, Canada, Cuba, Germany, Austria, France, the British Isles, Russia and Australia.) In 1911, 6,000 cases occurred in Sweden alone. Of all cases, 96 per cent occur before the 10th year of life, 90 per cent before the 5th year, and over 75 per cent during the first 3 years of life (Ed. Müller). The well-to-do families are affected just as often as the poor. Race has no effect on disposition.

Contagiosity.—The disease always comes from a preëxisting human case, either directly or indirectly. There is no evidence that it is spread by water, milk, fruit or other foods. As the virus resists drying, it is possible that it may be spread by inanimate objects (*fomites*), that have been contaminated by a person sick of the disease, or by a healthy carrier. It is asserted that the dust from the sick-room injected into monkeys will give rise to the disease (Neustadler and Throo, 1911). Again, it is said that shoemakers or their children are often affected (Eichelberg). Further, Hill, in Minnesota, found that cases of poliomyelitis were most common on dusty streets; but Lovett and Sheppard (1914) could make out no relation to dust. Other points in favor of the possibility of infection by *fomites* are (1) the infection of monkeys by extracts of handkerchiefs used by poliomyelitis patients (Josefson); (2) the entrance of a new family into a house in which there had been cases of poliomyelitis has been followed by cases of the disease among the incomers.

As to transmission by insects, the frequency of the disease in August and September, the proof that flies may be contaminated by the virus and the latter retain its virulence for at least several days (Flexner and Clark; Howard and Clark), the experiment in which the stable flies (*Stomoxys calcitrans*) were allowed to suck blood from paralyzed monkeys and to bite healthy monkeys, transmitting the disease (Rosenau; Anderson and Frost), are among the points of evidence adduced in its favor. But none

of these is convincing. Against the view are the following facts: (1) *Lice and mosquitoes do not, on biting infected monkeys, become contaminated with the virus* (Howard and Clark); (2) *the virus is rarely present in the blood;* (3) *epidemics, though commonest in autumn, may also occur in mid-winter;* and (4) *the disease may break out miles away from any other case, and so must be brought by human intermediators* (*Ed. Müller*).

Since (1) *the portal of entry* is, in all likelihood, the lymphatic tissue of the mouth, throat, nose and pharynx (possibly, also, of the intestine), (2) the virus remains for a long time virulent in the secretions from the mouth and nasopharynx of patients, convalescents, and healthy contacts, and (3) the disease undoubtedly develops in persons coming in contact with those infected or near the infected, it seems probable that *the transmission is ordinarily direct from one human being to another,* without the intermediation of *fomites,* or of insects. Whether this occurs by "droplet infection," or by immediate contact, or by both, we do not yet know.

Certain points still remain to be cleared up: (1) the marked prevalence of the disease in Northern climates; (2) the predominant prevalence in August and September; (3) the greater predisposition of people in country districts and in thinly populated areas; (4) the absence of tendency to contact infection among monkeys, when diseased and healthy are permitted to intermingle; and (5) the absence of tendency to infection among doctors, nurses, and laboratory experimenters working with the disease. It is probable that in every epidemic an enormous number of abortive infections occur and give immunity.

Prophylaxis.—This must be very difficult, if the ideas regarding direct transmission, above outlined, are correct. The danger from convalescents, from abortive cases, and from healthy contacts who become carriers, must be very great. The conditions seem to be similar to those in epidemic cerebrospinal meningitis.

Quarantine methods are worthless; the danger is less often from the actually sick than from healthy people around them (Wickmann; Wernstadt, 1911). Similarly, compulsory disinfection of linen, clothing, etc., offers but little hope, and seems hardly worth while.

In epidemic times, the schools should be closed; at any rate the sibs of affected children should not be permitted to go to school, as they may act as carriers. Children's parties should not be held. Funerals after deaths from poliomyelitis should be private.

When the disease is prevalent, each child should have its own handkerchief, and should never use the handkerchief of another child, or that of a parent. Towels, handkerchiefs, etc., used by patients should be sterilized by boiling. House disinfection is advisable after poliomyelitis, though it is probable that the inmates have become carriers through contact.

Mouth washes are of doubtful efficacy. If one is used at all, probably a 1 per cent solution of hydrogen peroxid is best; if desired, 2 per cent potassium permanganate may be added.

Symptoms.—The incubation period varies from 5 to 10 days, averaging a week. Exceptionally it may be shorter, 1-3 days, or longer, 15 days. In monkeys it averages about 10 days, but may last 33 days (Flexner and Lewis), or even 46 days (Leiner and von Wiesner).

The children sicken with signs of an infection often taken to be tonsillitis or influenza. There may be vomiting, diarrhea, slight fever, accelerated pulse, sweats, mental dullness, sometimes an exanthem, rarely herpes labialis (in contrast with cerebrospinal meningitis), occasionally herpes zoster, and, very rarely, convulsions; at first there may be signs of meningeal irritation, with rigidity of the neck, and general cutaneous hyperesthesia, suggestive of meningitis. Usually there is a leukopenia (3,000-8,000 W.B.C.); occasionally, a leukocytosis (10,000-30,000). At this time the cerebrospinal fluid shows but few changes; it is clear; the pressure is increased; the protein content is high; there is slight lymphocytosis, and cultures are sterile—findings in marked contrast with those in cerebrospinal meningitis.

In from 1 to 7 days later, the paralytic stage is entered upon; in the SPINAL FORM, paralysis is noticed in one leg, or arm, or in two, three, or four extremities simultaneously. The lower extremities are involved in about four-fifths of the cases (E. Müller). The M. quadriceps and the Mm. peronei are most often involved, the muscles of the shoulder girdle and the abdominal muscles frequently. Paralysis of the diaphragm and of the intercostal muscles may occur. The muscles innervated by the cerebral nerves are sometimes, though rarely, paralyzed. Occasionally, there is paralysis of the muscles of the neck and back; the child's head droops, or he "falls together in a heap."

It is characteristic of the paralysis in the Heine-Medin disease that it assumes its full development immediately, having its widest distribution, usually, at the time of its first appearance. It is a lower motor neuron paralysis (flaccid; reaction of degeneration at the end of a week; loss of reflexes). The deep reflexes are lost, if the muscles concerned are paralyzed; otherwise they, and the cutaneous reflexes, are usually unaltered. The sphincters are normal. The findings in the cerebrospinal fluid at different stages of the disease, reported from the Hospital of the Rockefeller Institute, are interesting (*q. v.*).

The *stage of repair* now sets in, and continues for 1-1½ years. Within the first few weeks, there is usually a marked recovery from the paralysis, with concentration of the residual paralyses in certain groups of muscles (those in which the reaction of degeneration has been outspoken). In these residual paralyses, the topography usually corresponds to the segments of the spinal cord in which the anterior horn cells have been injured.

Later on, as a result of the degenerative atrophy, contractures develop in the antagonists of the paralyzed muscles and cause paralytic club-foot, flat-foot, etc. The bones remain backward in their development. Loose joints develop. Scoliosis or kyphosis may result. The affected extremity is cool, cyanotic, and often edematous for a time.

In the CEREBRAL FORM of the Heine-Medin disease, the clinical picture is that of an infantile cerebral palsy; undoubtedly some of the cases—not all—of the Strümpell type of acute hemorrhagic encephalitis are examples of the Heine-Medin disease. Occasionally a monkey manifests the cerebral form after experimental infection; a typical meningoencephalitis is then found on histological examination, the lesions being similar in type to those found in the spinal cord in the spinal form of the disease.

In the cases taking the FORM OF LANDRY'S PARALYSIS, we have to deal with a peracute and fatal form of the Heine-Medin disease (Wickmann). The paralysis begins in the lower extremities, quickly ascends, involving the arms and the bulbar centers, ending in death in a few days. Should the paralysis begin in the arms, it descends to the leg centers in the lumbar cord and ascends to the medulla and pons. Similar cases are met with in monkeys experimentally infected (Flexner and Lewis; Römer); in one monkey the paralysis advanced with great rapidity, and death occurred a few hours after the paralysis was first observed.

In the BULBAR AND PONTINE FORMS of the Heine-Medin disease, the involvement of the cerebral nerves dominates the clinical picture. The nucleus N. facialis is most often injured usually on one side only, and frequently with simultaneous involvement of the nucleus N. hypoglossi—a true poliomeencephalitis inferior. More rarely, the nucleus N. oculomotorii, the nucleus N. trochlearis, and the nucleus N. abducentis are injured (poliomeencephalitis superior). The motor nucleus of the N. trigeminus may be attacked; the nuclei of the other motor cerebral nerves (N. vagus, N. glossopharyngeus, N. accessorius) are but rarely affected. In the experimental disease in monkeys, the results resemble the disease in human beings. In all the bulbar and pontine forms, there is usually some simultaneous spinal paralysis.

In the ATAXIC FORM of the disease (Medin), the clinical picture resembles that of Friedreich's ataxia (*q. v.*). It is due to lesions of the cerebellum or of the cerebellar paths in the spinal cord, the medulla oblongata, the pons or the mid-brain. As far as I know, this form has not yet been reproduced in monkeys. It seems likely that some of the cases of "acute ataxia in children" described by neurologists are instances of unsuspected Heine-Medin disease.

In the so-called POLYNEURITIC FORM of the disease, the symptoms are those of a multiple neuritis (pains, paresthesias, paralysis), but in cases that come to autopsy, the actual lesions are found to be *meningomyelitic*.

I saw a remarkable example of this type in 1906 with Dr. G. H. Field of Cobourg, Ontario. The patient, a young girl, after an attack resembling influenza with sore throat, began to have excruciating pains all over the body with extreme cutaneous hyperesthesia and sweats. She would cry out when her bed was approached. After a few days there was paralysis of both legs and partial paralysis of one arm. We made the diagnosis of acute "anterior poliomyelitis, complicated by multiple neuritis." The child recovered though there is considerable residual paralysis.

In the MENINGITIC FORM, the symptoms due to the meningeal infiltration dominate the clinical picture. The rigidity of the neck, the pain in the back, the tendency to opisthotonos, the positive Kernig's sign, the headache and the vomiting all point to meningeal irritation. A meningitis does exist but it is only a part of the general meningomyelitic process. Cytodiagnostic and bacteriodiagnostic methods applied to the cerebrospinal fluid (*q. v.*) quickly differentiate.

In the ABORTIVE FORMS of the Heine-Medin disease, first recognized by Wickmann, no outspoken paralyses occur, though the prodromal symptoms may be present to a greater or less extent, (fever and sweating, with symptoms suggesting a respiratory, a gastro-intestinal, a meningeal, or a general influenzal infection). One sees every transition between these forms with no paralysis, through the forms in which there are transitory slight pareses of one or of several muscle groups, or temporary loss of deep reflexes—the so-called "rudimentary poliomyelitis" of E. Müller—to the outspoken monoplegias, paraplegias, and quadriplegias.

It is now believed that in large epidemics of the Heine-Medin disease from $\frac{1}{3}$ to $\frac{1}{2}$ of all the infections are abortive forms! These forms can now often be recognized by the clinician, especially if he resort to serodiagnostic methods. (See Diagnosis.)

Prognosis.—The mortality varies much in different epidemics, according to Wickmann from 10-42.3 per cent. It was formerly believed that the disease is rarely fatal; that belief was due to a failure to recognize the fatal cases as the Heine-Medin disease, physicians taking them to be cerebrospinal meningitis, Landry's paralysis, etc. Death, when it occurs, usually takes place on the 4th or 5th day. The mortality is greater in adults (*poliomyelitis acuta adultorum*) than in children (2 or 3 to 1). A great many patients recover without any residual paralysis. In children this is true of nearly half the cases; in patients over 11 years old, of about $\frac{1}{3}$. In Lovett and Sheppard's experience, 13.5 per cent of all the paralyzed cases ultimately recovered completely, without residue. Wickmann assures us that we can count on 20 per cent of complete recoveries without residue in the cases suffering from paralysis.

The mortality is much greater among inoculated monkeys: With ordinary virus $\frac{3}{4}$ of the animals die; with passage-virus, the mortality approaches 100 per cent (Flexner and Lewis; Römer).

Pathology.—This has been carefully studied and described. In 1870, Charcot studied the after effects (loss of anterior horn cells). In 1888, Rissler made a study of fresh cases, at autopsy Recently, human and monkey tissues have been studied with great care, especially by Flexner and his co-workers, who have shown that the process involves the organs of the body as a whole, and that the involvement of the anterior horns is incidental to this general process. The virus injures and destroys the ganglion cells of the anterior horns, partly by direct intoxication, but chiefly through local perivascular, lymphangitic changes. In the nervous system, the lesions are those of a widely disseminated meningoencephalomyelitis. Batten (1904) had attributed most of the paralyses to thromboses in the anterior spinal arteries.

A peculiarity of poliomyelitis lies in the fact that it is an acute perivascular inflammation with lymphocytic infiltration, not limited to the anterior horns (though predominant there), but involving also the arteries and veins in different parts of the gray matter, including the posterior horns and the spinal ganglia; in the nervous system, the lesions are those of a widely disseminated meningoencephalomyelitis. The infection, as we have seen, *spreads* through the perineural and perivascular lymph vessels. Macroscopically, there may be but little to be made out; but microscopically, the histological changes are so extensive that one wonders that the clinical symptoms are not more pronounced than they are. The infiltration of the pia, the dilatation of the veins in the gray matter, the perivascular accumulations of small mononuclear cells, the neuronophagy of the anterior horn cells, make a characteristic histological picture. The swelling of the mesenteric lymph glands, of Peyer's patches and of the solitary follicles in the intestine is emphasized by Flexner, Peabody and Draper, who have made a report on the visceral lesions of human cases. It is remarkable that such a disseminated infiltrative lymphocytic inflammation, involving so many tissues throughout the body, should, in the majority of cases, give rise to a clinical picture simulating a "system-disease" of the spinal cord (anterior horn cells). It is probably simply owing to the richness of the anterior horns in blood-vessels and in lymphatics that these cell-bodies of the lower motor neurons are picked out.

Diagnosis.—This is easy enough in the spinal form after the paralytic symptoms have appeared, and it may be suspected, and made earlier in epidemics, from the presence of fever, sweats, general hyperesthesia, and the findings in the cerebrospinal fluid above described. The disease in its earlier stages and in the atypical forms is most often mistaken for influenza, polyarthritis, polyneuritis, muscular rheumatism, meningitis, gastroenteritis, typhoid fever, or meningism.

In the early stages, the general hyperesthesia is characteristic. There is a tendency to profuse sweats. The [illegible] or, at any rate, absence of [illegible] is quite [illegible]. The sleepiness in the daytime, with restlessness at night, the diminished muscle tonus, and the early loss of reflexes in limbs that later become paralytic, and of the abdominal reflexes, are important early signs. The forms other than the spinal form are very often incorrectly diagnosed.

Serodiagnosis of the Poliomyelitis Virus.—As in case of [illegible], [illegible] as a specific test are to be drawn are somewhat [illegible]. [illegible] bodies are present, which [illegible] in the [illegible]. Flexner and Lewis, Wilson and

E. Müller, *et al.*); in the serum of human beings that have not had the disease, these specific antibodies are not present (Kling and Levaditi). By serodiagnosis, therefore, we have a method that permits us to decide whether a person has had the Heine-Medin disease earlier or not, for the antibodies are very persistent, remaining active in the blood certainly for many years after the infection, perhaps through the whole of life. By serodiagnosis, it has been proved (1) that sporadic cases that recover have the same antibodies as those that occur in epidemic cases, the etiology of the two therefore being doubtless identical (Netter and Levaditi); (2) that after abortive attacks, the antibodies are present in the blood, just as after severer attacks, a fact of great importance for epidemiological studies (Römer); (3) that among healthy contacts, the blood in many instances contains the antibodies (Kling and Levaditi), thus supporting the view that in epidemics a large number of people have a mild infection and acquire immunity without knowing anything about it; and (4) that some cases of the Strümpell type of acute encephalitis in children have been infections with the virus of Heine-Medin disease (Müller and Römer).

This method involves mixing some of the serum to be tested with an amount of virus known to be capable of producing the disease in a monkey. If on injection of the mixture into a susceptible animal the disease does not develop it is assumed that the virus has been neutralized by immune bodies in the serum.

Differential Diagnosis.—We differentiate the disease (1) from *meningitis,* meningococcal, pneumococcal, influenzal, or tuberculous (cytodiagnosis and bacteriodiagnosis on lumbar puncture, greater rigidity of neck and spine, severer headache, changes in eye grounds, greater disturbance of consciousness); (2) from *influenza* (catarrhal phenomena more in the foreground, rather than the pain and hyperesthesia; sputum); (3) from *scarlatina with angina* (may be impossible to differentiate early; later, serodiagnosis). Later in the disease, we have to distinguish poliomyelitis (4) from true *polyneuritis* (slower development, paralyses not complete at beginning, edema occurs earlier, objective sensory disturbances usually more marked and last longer, cerebral nerves more often involved, peripheral nerve topography rather than radicular topography of paralysis, paralysis more distal in extremities and often bilaterally symmetrical); (5) from other forms of *acute myelitis* (involvement of pyramidal tract and sphincters, sensory disturbances); (6) from *amyotonia congenita* (q. v.); (7) from *paresis in rickets* (slower onset, non-febrile); (8) from *hematomyelia* (afebrile, dissociated anesthesias); (9) from *cerebrospinal lues;* and (10) from *progressive muscular atrophy.*

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E. Other Diseases Due to Filtrable Viruses

1. Foot and Mouth Disease

The filtrable virus of Loeffler-Frosch is the cause of **foot and mouth disease** (stomatitis epidemica), which sometimes attacks human beings. Siegel asserts that he finds extremely minute coccoid bodies in the lesions. The disease is most often contracted by young children through raw milk. In persons coming into contact with infected cattle, pigs, sheep or goats, the transmission may be direct.

After certain prodromata (fever, headache, pains in the limb, anorexia, constipation, nausea, and dry mouth), red spots appear on the mucous membrane of

the mouth. These soon become vesicular with contents serous at first, later, turbid. The tongue swells and there is salivation. In a few days, the vesicles rupture, leaving superficial ulcers behind, which as a rule soon heal. The fingers and toes may show vesicles also. Most patients recover.

In 1915 one of the students at the Johns Hopkins Medical School developed the disease in typical form. The case has been carefully described in the paper by Dr. P. W. Clough.

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2. Pappataci Fever

The *filtrable virus of Doerr and Russ* is the cause of the three-day fever which occurs on the shores of the Adriatic known as *pappataci fever;* it is transmitted through the bite of a gnatlike dipterous insect (*Phlebotomus pappatacii*). The disease may be mistaken for abortive typhoid or for mild undulant fever.

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3. Transmissible Sarcoma

The *filtrable virus of Peyton Rous* has been shown to be capable of reproducing **sarcoma** in mice; thus far, we are not sure of the existence of this virus in sarcomatous human beings.

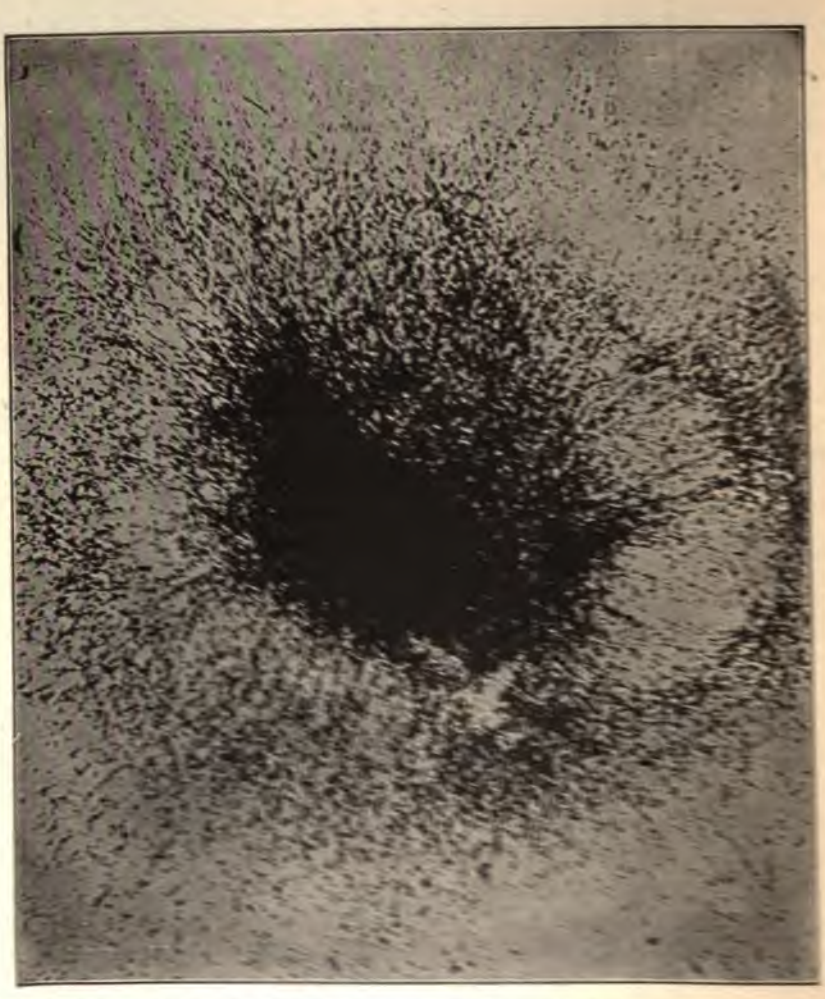

Fig. 124.—Culture of the Ehrlich Rat Sarcoma. The Central and Completely Opaque Mass is the Original Tumor Fragment. The New Cells are Arranged Irregularly Throughout the Surrounding Medium-Hematoxylin Stain. (After A. Carrel and M. T. Burrows, "Studies from the Rockefeller Inst. for Med. Res." Reprinted from J. Exp. Med.)

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IV. DISEASES DUE TO UNKNOWN INFECTIOUS AGENTS

Under this heading will be discussed (1) The Acute Exanthemata, and (2) Mumps.

A. The Acute Exanthemata

The acute exanthemata include (1) scarlet fever, (2) measles, (3) rubeola, (4) the fourth disease, (5) chickenpox, (6) smallpox, (7) sweating sickness, and (8) Rocky Mountain spotted fever.

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1. Scarlet Fever (Scarlatina)

Definition.—A highly contagious disease of unknown etiology, accompanied by sore throat, a diffuse red eruption on the skin, and often followed by acute glomerulonephritis.

Etiology and Epidemiology.—Scarlet fever has been known since the epoch-making descriptions of the London epidemics of 1661-1675 by Sydenham. The disease often occurs in epidemics, which vary greatly in severity. Some epidemics are so mild that they are not recognized as scarlet fever at all, though the next year the epidemic may be of a much more virulent type. They are most common in autumn and winter, rare in summer. Sporadic cases are common. Susceptibility to the disease is far less general than in measles.

The most important predisposing factor is age, over 85 per cent of the cases being in children before the age of puberty.

The source of the infective agent is not positively known, but it is believed that the disease is spread through the nasal, oral, and bronchial secretions of infected persons, and probably mainly through desquamated scales.

The infective agent is unknown. Some believe it to be a streptococcus; others assume a protozoön invasion (*Cyclosterion scarlatinæ* of Mallory; *Chrystanzoön scarlatinæ* of Gamalia; leukocytic inclusions of Döhle).

The virus is very resistant to light, to heat, and to drying. It may be transmitted by contaminated *fomites*, or through a third person; but most often the disease is acquired by direct contact with a patient suffering from scarlet fever. A child is a menace to others for at least 6 weeks from the beginning of the disease, in some cases for a much longer period. The disease is spread largely through the schools, and especially by mild cases often incorrectly diagnosed as German measles.

Symptoms.—The *incubation period* varies from 1 day to 1 week, averaging 3-5 days; it may be as long as 14 days. The *onset* is sudden, with fever, vomiting, and often convulsions; there is tachycardia, sore throat, and enlargement of the glands at the angle of the jaw. Within 24 hours, a *red macular eruption* appears on the neck, and on the upper part of the chest; later, this exanthem involves the skin diffusely, the whole body quickly becoming affected, except for areas around the lips and chin, and sometimes the extensor surfaces of the extremities. The *typical scarlatinal eruption* is an intense livid hyperemia, often mottled with petechiae. Often transverse pale lines are seen at the flexor surfaces of the elbows, knees, etc. A common finding is a red, punctiform mottling of the mucous membrane of the hard palate and of the skin in the armpits and groins. Sudaminal vesicles are common.

I would emphasize especially the appearance of the eruption at the *beginning*. It appears as small spots, separate from one another, at first of a light rose color, but soon becoming closely crowded together, and of a deeper red color. The spots become so numerous that on superficial examination, the skin may look evenly red; they do not really become confluent but remain separate. This is best made out by looking at a fiery red area and then making it disappear by pressure and watching its reappearance after the presssure is removed; the single red spots then reappear quickly, and soon the almost uniform redness is regained.

If, with the handle of a percussion hammer, a line be drawn over the red skin, a sharp white line arises, due to vasoconstrictor spasm, and only slowly disappears; this is the *raie blanche* of French writers.

The eruption lasts 3 or 4 days, and then gradually fades. The *desquamation*, usually beginning on the neck and trunk, is especially marked on the palms of the hands and the soles of the feet, where the skin may be shed in lamellae; it occurs from the end of the first, or the middle of the second, week on. The *"strawberry tongue"* is characteristic (4th or 5th day), a furred tongue through which the swollen red papillae are seen. The throat generally shows evidences of an *acute angina;* there may be congestion, congestion with edema and tonsillitis, or a membranous inflammation, involving pharynx, tonsils and uvula, presenting, with the cervical adenitis, a picture quite like that of a true diphtheria. The *temperature* is remittent during its course; it falls by lysis with the efflorescence of the rash, becoming normal about the 9th or 10th day. The tachycardia

(120-180) and tachypnea are generally in proportion to the pyrexia, or greater. The spleen is frequently enlarged slightly. In severe cases, delirium and extreme prostration are alarming. In mild cases the subjective symptoms are slight. Hemorrhagic, fulminant and anginose, abortive cases, and even cases without eruption, occur. *Polymorphonuclear leukocytosis* is the rule, high in severe cases, 30,000-60,000; there is usually some *eosinophilia.* The urine shows the ordinary febrile characteristics in uncomplicated cases, but it should be examined daily. It is to be remembered that at the height of the disease, a trace of albumin and a few casts need not indicate a serious nephritis. Epigastric disturbances, except constipation, are uncommon after the initial vomiting, unless uremia due to a complicating nephritis supervene.

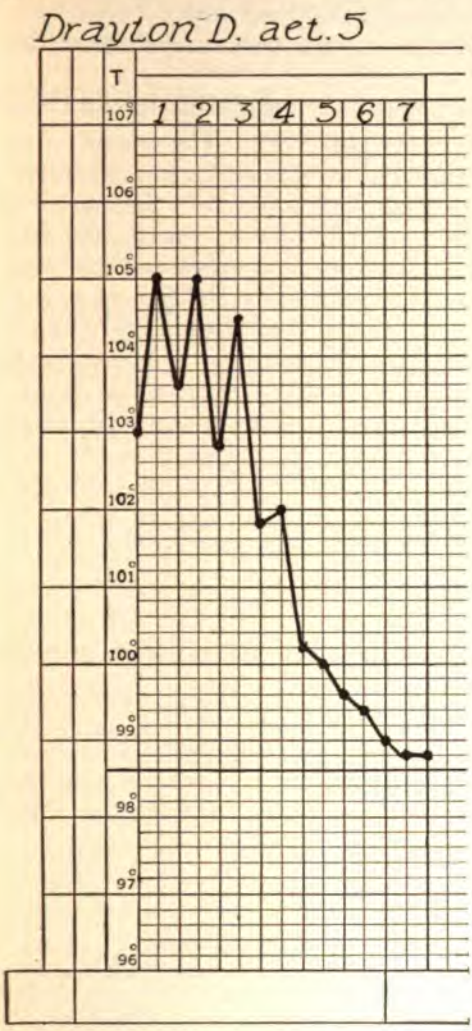

Fig. 125.—Scarlet Fever.

The condition long known as *surgical scarlatina* is not truly a scarlatina in the medical sense of that term, but is probably an erythema due to sepsis following infection of a wound.

One attack of scarlatina generally confers immunity; reinfection occurs in 1 out of 500 cases. Relapse is rare.

Complications and Sequelae.—These include: (1) streptococcus angina; (2) streptococcus sepsis; (3) otitis media; (4) scarlatinal polyarthritis; (5) nephritis (8-22 per cent); (6) endocarditis. These are nearly all complicating infections with streptococci; nephritis and adenitis are due to the virus of the disease itself.

In the 3rd or 4th week, or even later, a recurrence in the form of an *acute hemorrhagic glomerulonephritis,* and with it fever, angina, and a *postscarlatinal adenitis* (Schick) not infrequently develops. These post-

scarlatinal affections have also been carefully studied by Pospischill and Weiss (1911).

Prognosis.—The mortality varies greatly, 5-30 per cent. In the very mild epidemics, there may be no deaths; in the severer epidemics, the mortality may be very high.

Diagnosis.—This is easy in well-marked cases, but is difficult, and sometimes really impossible, in mild and in atypical cases. The disease must be differentiated (1) from *measles* (period of incubation longer, characteristic prodromata, rash later and papular with crescentic distribution, Koplik's spots); (2) from *diphtheria* (bacteriology of throat; the two diseases may coexist); (3) from *German measles* (afebrile; rash; other cases in epidemic); (4) from the *initial erythemas* in typhoid, pneumonia, smallpox, and influenza; (5) from *drug-rashes* (antipyrin, quinin, atropin); (6) from *serum rash* after antitoxin administration; (7) from *acute exfoliative dermatitis* (absence of throat symptoms, no strawberry tongue, hair and nails affected; the disease is recurrent); and (8) from *Vincent's angina* (stained smears show spirilla and fusiform bacilli).

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2. Measles

(*Morbilli, Fr. Rougeole, Ger. Masern*)

Definition.—An acute, specific, infectious, and extremely contagious disease, characterized by catarrhal inflammation of the upper respiratory tract and by a characteristic exanthem.

Etiology.—The infective agent must be a living contagium, but is as yet wholly unknown. Blood cultures in ascitic fluid are negative after 24 hours in the thermostat, but if a healthy person who has not had measles be then injected with the mixture of blood and ascitic fluid, he develops typical measles (L. Hektoen). The unknown virus is present also in the secretions from the eyes, nose and mouth, in the sputum, and in epidermal scales. "Droplet infection" is probably an important mode of transmission. Persons coming down with the disease may communicate it to others from 3 to 5 days at least before their own eruption appears. The virus is incapable of long survival outside the human body, in marked contrast with the virus of scarlet fever. The disease passes directly from human being to human being, being rarely, if ever, transmitted by *fomites*. It is asserted that a room vacated by a measles patient, if it be simply well-aired for 24 hours, can be occupied next day by susceptible persons without danger!

Measles, in epidemics, spreads with extreme rapidity. New epidemics often break out in schools immediately after vacations. Children from 1 to 5 years are most often infected, but the disease may occur at any age except in sucklings up to the 4th or 6th month. It seems to be a children's disease, simply because nearly everybody is attacked in childhood and has immunity afterward. One attack usually yields permanent immunity, though undoubted instances of 2 and 3 attacks are on record. Natural immunity is extremely rare; the result is that it is very unusual for a human being to escape from measles; he is almost sure to contract the disease at some time or another during his life. The disease is less common in summer. Sporadic cases may be met with at any time.

Symptoms.—The *incubation period* is said to be exactly 11 days, though in rare instances, it varies from the rule, lasting only 7, or as long as 18 days.

The *prodromal stage* lasts 3 days; coryza, photophobia, conjunctivitis, a dry, troublesome cough, with hoarseness, moderate fever, anorexia, malaise, appear. The face and eyelids look swollen; the eyelids stick together in the morning. The diagnosis at this stage may not be [illegible] unless measles is epidemic and one is on the lookout for cases. Usually before the appearance of the exanthem, there is a characteristic [illegible] of the mucous membrane of the mouth and pharynx (irregular, [illegible]

ark red macules, especially common on the uvula, and soft palate appear). ut in addition, thanks to the New York pediatrist, Koplik, we now have sign that often permits the making of a positive diagnosis in the pro-romal stage, or even in the last two or three days of the incubation period. eculiar white spots, now generally known as "KOPLIK'S SPOTS," appear n the buccal mucous membrane opposite the molar teeth, or on the inside f the lips, or at the junction of the gums with the cheeks. They are ightly elevated, white or bluish white, sharply circumscribed round spots, ie size of the head of a pin, or smaller, surrounded by a slight zone of edness; they cannot be wiped off; a scraping examined microscopically ows only epithelium and detritus. It is as though the red mucous mem-rane had been touched here and there with a little white paint on the p of a fine camel's hair brush. As they grow older, the spots increase in ze, and become more prominent; they disappear, in from 2 to 5 days, ithout residue; 6 to 20 such spots are often visible. They never occur i scarlet fever, or in other exanthematous diseases, though some assert iat they are seen occasionally in German measles. They are easily dis-nguishable from thrush or from aphtha; I consider them of great diag-ostic importance for the early diagnosis of measles; they are present in x-sevenths of all cases (Heubner). Occasionally preceded by prodro-ial erythema, the characteristic skin eruption appears on the 14th day fter infection, that is, 3 days after the prodromata begin. It is a ACULOPAPULAR ERUPTION, often grouped, appearing first on the face sometimes first on the soft palate), scalp, and in front of and behind ie ears, thence extending to the neck, the upper trunk, and upper arms, hen to the lower trunk, the buttocks and thighs, and finally to the other ortions of the extremities. The full development is reached in 2-2½ days, ut the symptoms do not disappear with the appearance of the eruption. There is a characteristic variegated mottling of the skin. The color of he exanthem is at first pink, and the measles are small, rounded or irregu-ar, though sharply circumscribed; the color, later, becomes of a darker red, nd is often copper-colored or brownish-red. The outlines grow less dis-ct, and become very irregular, adjacent measles often fusing with one ther. If, inside the spots, the sebaceous glands become swollen, the a becomes elevated (*morbilli elevati*); sometimes this swelling does appear (*morbilli læves*). Occasionally there are capillary hemor-ges (*hemorrhagic measles*).

The *fever* during the 3 days of prodromata is remittent and of variable ght; it then falls, but rises again as the eruption appears and may be h. The pulse and the respiration are accelerated.

The *blood* in measles has been carefully studied by Hecker. There e typical changes, which precede the Koplik spots by from 2-6 days. leukopenia (3,000-4,000) appears, with a relative and absolute decrease f the number of lymphocytes, and relative increase (though slight abso-

lute decrease) of the polymorphonuclear neutrophils; the eosinophils are decreased during the prodromal stage, and vanish entirely during the eruptive stage. This *incubatory leukopenia* may be of real importance for early diagnosis. Slight enlargement of the lymph glands can be made out. During the exanthem, the catarrhal symptoms grow worse; the general condition changes, the child will not eat, grows apathetic, and often dull and delirious. The tongue is coated; the bowels are constipated; the urine is scanty and high-colored.

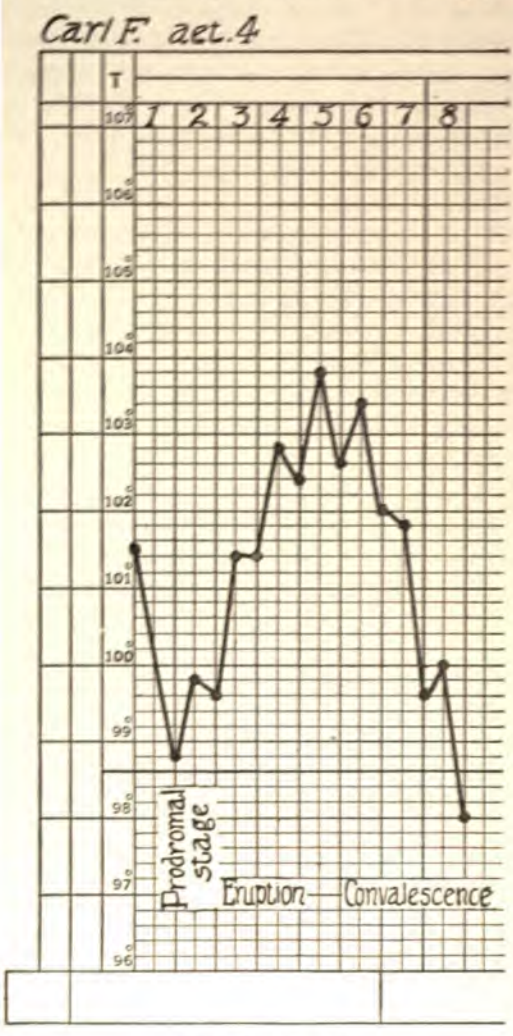

Fig. 126.—Measles.

The eruption lasts from 3 to 5 days. The temperature often falls by crisis, after a precritical rise, and, in a few hours, the child seems remarkably improved; he breaks out into a sweat, falls into a sleep; on waking the psyche is clear, the cough is looser, and the appetite begins to return. Sometimes this critical change is not seen, the temperature, instead, falling by lysis during 1-2 days of defervescence. As the eruption fades, *bran-like desquamation* sets in during the fading, whereas, in scarlet fever, the lamellar desquamation does not appear until a week after the rash has faded. During the last stage, the patient should be most closely watched and most carefully nursed, for the danger of complications and is very great. Chilling of the body surface, especially, is to b and the presence of any tuberculous person in the proximity of should be prohibited. During convalescence, there is often a bradycardia, sometimes cardiac arhythmia.

Abortive cases and *afebrile cases* are known, as well as ***measl an eruption.*** Sometimes the rash begins in the usual way, the

indistinct, and the patient's general symptoms grow more severe. This form is much feared by the laity, who speak of the measles "striking in." In these cases, the skin is usually pale and cyanotic, due to cardiac weakness and to dyspnea due to swelling of the bronchial mucous membrane; unless the skin can be made hyperemic by a mustard pack, and the circulatory conditions improved, the outlook is grave.

The eruption in measles has recently been especially studied by von Pirquet. During *the first day of the eruption*, the first signs appear in the form of scattered red papules on the head and trunk, usually first behind the ears and in the middle of the upper back, then around the mouth and nose, on the cheeks, in front of the ears, and on the forehead, with possibly a few upon the chest and abdomen.

During the next two to four days, the eruption spreads over the whole body. At the beginning of the *second day*, there is an abundant eruption on the head and back, as far down as the crest of the ilium. The face, in its upper and middle parts, is intensely inflamed, though the cheeks still show only a scanty eruption. The eruption is also scanty on the chest, abdomen, shoulders, and medial sides of upper arms. A few papules can be seen on the arms, thighs, popliteal spaces, nates, and anterior surface of the legs. The posterior surface of the legs, the feet, the knees and elbows are still free.

At the beginning of the *third day*, as a rule, the eruption is intense on the head, trunk, shoulders, and anterior surface of the upper arm and of the thigh. It may also be intense, though less constantly so, on the dorsal surface of the upper arms, the forearms, and the posterior surface of the thighs. A scanty eruption is seen in the popliteal spaces, on the legs, on the hands and knees, sometimes on the nates. A beginning eruption is visible on the feet while the elbows still remain free. By the *fourth* or the *fifth* day, the exanthem is, as a rule, fully developed, except perhaps on the nates, feet and elbows.

As the eruption fades, the rose-red color of the first two days diminishes, and the rash becomes slightly pigmented. The *fading* begins, constantly, on the forehead, usually at the beginning of the *second* day. By the beginning of the *third* day, the rash on the forehead and the hairy scalp has faded much, and the rash on the rest of the face, the trunk and the shoulders has begun to fade. By the beginning of the *fourth* day, the fading has advanced to the rash on the extremities. The slight pigmentation on the forehead and hairy scalp has now vanished. By the beginning of the *fifth* day the head, with the exception of the cheeks, has lost all traces of the exanthem, while the pigmentations on the rest of the body following the rash are still distinct. The elbows and feet often remain entirely free from rash, more rarely also the knees, nates and hands.

Von Pirquet concludes that the temporal features of the rash stand in definite relation to the cutaneous arterial supply, the rash appearing earliest on those parts of the skin in which the arterial distance from the heart is least, and the circulation liveliest.

He believes that the exanthem depends upon antitoxic reactions to the measles virus in the cutaneous capillaries, in areas of the skin saturated with antibodies. He suggests that the freedom from the rash of the elbows, feet and nates can be explained by assuming that at the time when the most poorly arterialized parts of the skin become saturated with antibodies, all the measles germs have been removed from the blood by fixation (agglutination) in other capillaries of the body. (Cf. von Pirquet, "Das Bild der Masern auf der äusseren Haut," Berlin, 1913.)

The *course* of the disease is usually favorable if there are no complications. The public does not realize, however, how serious a disease measles is; various complications are possible.

Complications of Measles.—These include capillary bronchitis, broncho-pneumonia, necrotizing pneumonia, otitis media, and enteritis with diarrhea as the more important. Occasionally, severe inflammations of the eye, of the larynx (measles croup), or of the mouth (noma) are met with. Nephritis is very rare.

Tuberculosis after Measles.—Many children develop rapid tuberculosis after measles, the infection apparently lowering the resistance against the tubercle bacillus. If a cutaneous tuberculin reaction is positive before a measles infection, it becomes negative during the measles (von Pirquet), owing to disappearance of antibodies (ergins). Many a child, during convalescence from measles, develops an acute miliary tuberculosis, or a tuberculous meningitis; a flare-up in tuberculous mediastinal glands, or of pulmonary tuberculosis, is very common after measles.

Concurrent Measles.—Measles may occur simultaneously with scarlet fever, with diphtheria, with whooping-cough, or with chickenpox, in the same patient. When whooping-cough and measles occur simultaneously, the danger of capillary bronchitis is very great, especially in young children; the danger of subsequent tuberculosis is also increased. Varicella, in companionship with measles, is prone to give rise to deep ulcers and necroses of the skin.

Diagnosis.—In the *prodromal* stage, the acute catarrhal symptoms with leukopenia are suggestive, and the Koplik spots are decisive. In the *stage of eruption,* the disease must be distinguished (1) from *scarlet fever* (not mottled, non-papular, area about mouth free); (2) from *German measles* (rash not distinctly papular, lighter color, not confluent, often rudimentary, often afebrile); (3) from the initial rash of *smallpox* (severe general disturbances, higher fever, absence of Koplik's spots, nodular eruption later, rapid fall of temperature on appearance of exanthem); (4) from *typhus fever* (absence of Koplik's spots, character of eruption, higher temperature, course); (5) from *serum-exanthems* (anamnesis, accompanying phenomena); (6) from *drug-exanthems;* (7) from *exanthems in sepsis* (blood culture).

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3. Rubeola

(German Measles, Röteln)

Definition.—A benign, contagious, exanthematous disease, in which the skin eruption sometimes resembles measles, sometimes scarlet fever, though the disease is different from both.

Etiology.—The cause is unknown, but it is undoubtedly some infectious agent. The disease occurs in small epidemics, especially in children (2-10 years), but is common also in adults. Most people are susceptible, though

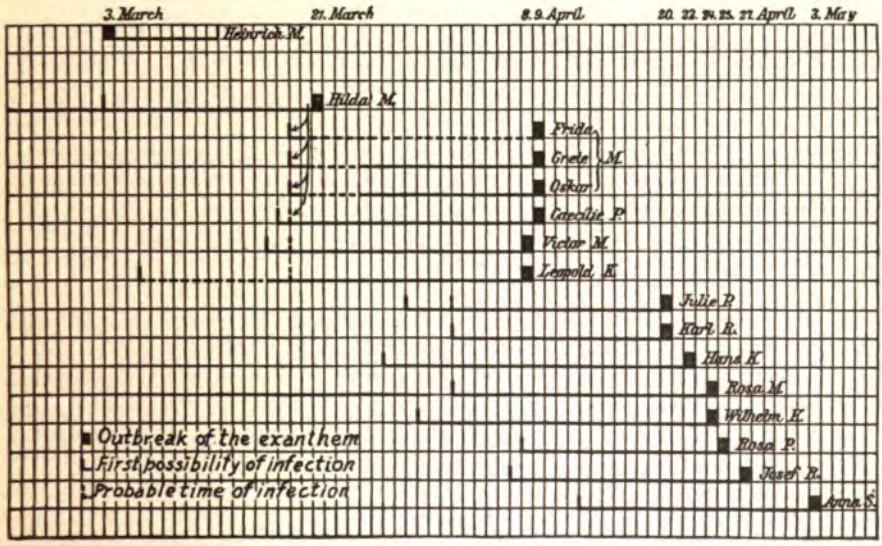

Fig. 127.—Diagram Showing the Maximal Incubation Period (21 Days) of a Small Epidemic of German Measles Breaking Out in a Hospital. (After B. Schick, "Ergeb. d. inn. Med. u. Kinderheilkunde," published by J. Springer, Berlin.)

there is not the universal susceptibility so characteristic of measles. One attack yields immunity.

Symptoms.—The *incubation period* varies between 2 and 3 weeks. The disease may resemble measles closely, but is milder in all ways; prodromata are often entirely absent. Sometimes there are mild catarrhal symptoms, as in measles; also headache, malaise and myalgias. *Koplik's spots are not present.* A fine, blotchy, *rose-red macular eruption* is quite constantly to be found on the mucous membrane of the throat. The skin eruption appears first on the face and scalp, and thence extends, *in crops,* over the rest of the body within 24-30 hours; it appears usually as small macules rather than as papules; these are rose-red and rarely confluent. When the eruption resembles that of measles very closely, it is called *rubeola maculosa;* when it resembles that of scarlet fever closely, it is called *rubeola scarlatinosa.* The confusion with scarlatina may be increased by swelling of the cervical, occipital, and retro-auricular lymph glands, often present. The eruption disappears entirely in from 1-3 days and is followed by fine desquamation, each crop following this course for itself.

Prognosis.—The disease is never fatal; complications are rare.

Diagnosis.—This is easy in epidemics; in sporadic cases, it may be impossible to tell it from measles on the one hand, or from mild scarlet fever on the other. When in doubt, it is best to deal with it as though it were the severer form of disease.

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4. Duke's Fourth Disease

This has been described by Duke as a disease separate from scarlet fever, measles, and rubeola. I do not think the evidence favors its existence as a separate entity. The cases so described have been, in my opinion, either rube scarlatina.

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5. Chickenpox

(*Varicella, Fr. Petite vérole Volante, Ital. Ravaglione*)

Definition.—An acute, febrile, contagious disease, of unknown etiology, characterized by a maculovesicular exanthem. The disease was formerly (by the "unitarians") believed to be a mild form of smallpox; since the European pandemic of 1868-1874, varicella and variola have been universally considered to be two separate and etiologically distinct diseases.

The Virus.—Lymph from a varicella vesicle, inoculated into another person who has not had the disease, gives rise to varicella, never to variola. Vaccination against variola does not protect from varicella. Varicella is rare except in childhood; variola may occur at any age. Inoculation of the rabbit's cornea with lymph from varicella is never positive; with lymph from variola it is always positive, and typical Guarnieri's corpuscles appear. The virus is probably acquired through direct contact, or through inhaling air near a patient. Rarely, infection is transmitted through a third person. Patients can infect others from the latter part of the period of incubation until the scabs are all thrown off. The virus, in contrast with that of variola, is not very resistant to atmospheric influences or to disinfectants.

Susceptibility.—The disease occurs chiefly before the 10th year of life; occasionally, a case is seen in the third decade, rarely later. Most children are susceptible. Epidemics are common. It never entirely dies out in large cities.

Immunity.—Most children have but one attack; cases of two and of three attacks in the same person are, however, known.

Symptoms.—The *incubation period* lasts from 2 to 3 weeks. There may be no prodromata; or malaise, anorexia, nausea, vomiting, and pains in the limbs may be present. The EXANTHEM appears first on the face and the hairy scalp, occasionally first on the trunk, and thence quickly spreads over the whole body. The quick spread is in marked contrast with the slow spread from above downward in variola. Flat, light red, spots appear; they are fairly sharply circumscribed and grow pale under pressure. They are variable in size and in form, though usually round or oval; in the latter case, the long axis is in the direction of the sulci in the skin. Thus, on the back, several may be seen in rows (convexity downward) on each side of the spine. Within 24 hours, a vesicle appears in the middle of each macule, and, enlarging to the size of a pea, becomes filled with fluid as clear as water. *These watery vesicles (crystalli), flat*

on the skin, surrounded by a narrow hyperemic zone, make the safest criterion for the diagnosis of varicella. They never occur in variola. From 10 to 200, or more, spots appear, irregularly scattered over the body; they are always discrete. A single vesicle, here and there, will be seen to be slightly umbilicated. After a few hours, the contents of a vesicle turn whitish, later pure yellow as the vesicle becomes a *pustule.* At the end of 2 or at most 3 days, the hyperemic zone vanishes and the contents begin to dry up to form a yellowish-brown *scab.* This scab falls off in a few days (8-10), usually leaving no scar. If itching be intense, as it frequently is, scars result from scratching. Pitting after varicella is said by some to be more common than after variola, but this is not at all true in my experience. Whether a scar follows or not, depends upon whether the corium is involved in the lesion. At the site of the lesion, there is *pigmentation,* which lasts for 2-3 weeks. Usually there are within 2-3 days successive *crops* of the exanthem, and it is a characteristic of this disease that *several, or all, stages of maturation of the lesion are to be found at one time.* If a varicella vesicle, or pustule, be pricked, the fluid does not all come out from a single puncture, because it is divided into several compartments. The septa run from the base obliquely upward to the middle of the surface of the vesicle; in the variola lesion, the septa converge from the surface, obliquely down to the middle of the floor (Unna). Cultures from the vesicle yield staphylococci; they have nothing to do with the etiology of varicella.

Along with the exanthem, there is also an *enanthem,* in at least one-half the cases (mouth, conjunctiva, nose, prepuce, meatus, vulva, anus).

Some of the vesicles may have a slightly *infiltrated base,* but this is never so firm, or so sharply circumscribed, as in variola.

A *prodromal rash* is sometimes seen, which may lead to the wrong diagnosis of scarlet fever; but the absence of sore throat, of the strawberry tongue and of swollen lymph glands, together with the subsequent course, quickly bring enlightenment. *Fever* is usually not marked, but persists after the appearance of the eruption. In mild cases, the whole process, including the separation of the scabs, is over in 6-7 days. In severer cases, with many vesicles and repeated crops, the duration may be 17-21 days.

Prognosis and Complications.—The mortality is very low. In marantic children, a gangrenous form sometimes occurs and may be fatal. Fatal sepsis, or metastatic abscesses, occasionally are met with, due to complicating pyogenic infection. The disease, like measles, predisposes strongly to tuberculous infection, and may accelerate one already under way. Hemorrhagic nephritis, and polyarthritis, are occasional complications. Hemorrhagic chickenpox, due to hemorrhagic diathesis, is rarely fatal.

Diagnosis.—This is usually easy. The disease must not be confused with smallpox, and should not be if the points emphasized above be duly considered.

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6. Smallpox (Variola, Ger. Blattern, Fr. Petite vérole)

Definition.—An acute, extremely contagious disease, of unknown etiology, characterized by a typical fever-curve and an eruption on the skin, which, during its maturation, passes through the stages of macule, papule, vesicle, pustule, and crust.

Occurrence.—This has become a relatively rare disease, considering the estimate that 25,000,000 people died of smallpox in 25 years in the 18th century, and 60,000,000 people during the whole of that century. The disease was observed in Mexico by the soldiers of Cortez in 1527; it has been brought in repeatedly from Europe and probably also from Africa (negroes). The disease has a very ancient history; prophylactic inoculation was used against it in China and India at least twelve centuries before the beginning of our time reckoning! The earliest report of an epidemic in Europe is that in the sixth century of our era (Marius Avenches). There appears to be no natural immunity against the disease, but compulsory application of Jenner's great discovery (1798-1800) of vaccination has made artificial immunity general. It is only when vaccination and re-vaccination grow lax that the disease reappears.

The Great Group of Pock Diseases.—Aside from syphilis (the "big pox"), and varicella ("chickenpox"), there is a large group of infectious diseases, affecting men, animals, or both, which stand in the most interesting reciprocal relations to one another. These diseases have been divided by Bollinger (1877) into two groups:

1. Those of epidemic, or epizoötic, distribution, with universal exanthem and transmission from person to person by a contagium which can be carried by the air (dust or droplets), and

2. Sporadic forms, in which the exanthem is localized in single, usually definite, parts of the integument, these occurring only through intentional or accidental inoculation, never by transmission of the contagium through the air.

To the first group belong, (a) VARIOLA, or the smallpox of man, and (b) OVINIA, or sheeppox. Goats are also susceptible to ovinia.

The second group includes (a) VACCINIA, or cowpox, (b) EQUINIA, or horsepox, and (c) local pock-diseases affecting other animals (rabbits, pigs, monkeys). Vaccinia and equinia were accidentally found in animals, and were, therefore, designated as "original" vaccinia or equinia. The other local poxes have been intentionally produced by the inoculation of animals.

Ovinia in sheep and goats is very much like variola humana.

Vaccinia occurs chiefly in milch cows, upon the teats of the udder. After several days of initial fever, papules appear upon the hyperemic skin, which later become vesicular, with contents clear at first, afterwards changing to pus; on drying, scabs are formed, which leave scars behind them when they fall off. The disease vaccinia lasts about 3 weeks, in cows.

Equinia in horses has a similar course, the process being localized on the skin of the fetlock of the hind foot.

By VARIOLATION is meant the intentional transfer of variola humana to men or animals by inoculation, that is, by transferring the virus from a human case to a superficial wound, intentionally made, in the person or animal inoculated. As virus, the serous contents of pock-vesicles or so-called lymph were chiefly used, though pus from pock-pustules and scabs was also employed.

Variolation of human beings is over 3,000 years old; variolation of animals was taken up by Jenner, when he made his studies on vaccinia. When a susceptible man is inoculated with lymph from a smallpox lesion, he develops variola humana, which, on account of its origin, is here designated VARIOLA INOCULATA. If, on the other hand, one inoculates a horse, or a cow, with the virus of variola humana, only a local disease results at the site of inoculation, and this local disease corresponds closely with, or is identical with, equinia or vaccinia, found accidentally originally, and designated as original equinia or vaccinia. Such local pock-diseases, resulting from inoculation, are called VARIOLA-EQUINIA and VARIOLO-VACCINIA, respectively, to show that they have been produced by inoculation of variola lymph, and not by transfer of "original" equinia, or "original" vaccinia. It is exceedingly interesting that, when lymph from such a variola-equinia or variolo-vaccinia is used to inoculate man, he in turn develops only a local eruption of papules, which become transformed into vesicles and pustules; he does not develop a universal exanthem, any more than when the lymph from an "original" cowpox or horsepox is used for the inoculation. If an inoculation "takes," in man, whether it be, on the one hand, from equinia or vaccinia, or, on the other, from variola-equinia or variolo-vaccinia, the person is, after the local process has run its course, completely or partially immune against variola humana.

If, still further, from a man so inoculated with variolo-vaccinia from a cow, we take lymph, and inoculate another cow, the local pock-disease that develops is called RETROVACCINIA; in the same way, a retro-equinia can be produced, and the lymphs from these in turn can also, when used on man, yield total or partial immunity against variola.

Similar experiments have been made with ovinia, and much is known about OVINATION and RETRO-OVINATION.

It seems very likely now that the cowpox and horsepox, "originally" found, were not independent diseases, but had resulted from accidental inoculations of "general pox" forms.

The different KINDS OF LYMPH in use include: (1) *variola lymph,* or the contents of the vesicles from human smallpox; (2) *vaccine,* derived from local cowpox; (3) *ovine lymph,* derived from sheeppox; and (4) *equine lymph,* from local horsepox.

Just what happens when human variola virus changes, in the cow or in the horse, is not known; it may be that mere *attenuation* occurs, though it seems more likely that *transmutation* is involved.

The evidence is against the possibility of a return from the transmuted to the original variola lymph; as far as we know, vaccine from the cow, inoculated into man, never causes variola, but always only vaccinia.

Etiology of Smallpox.—The view at present favored, is that which assumes a protozoön origin for the disease. The virus is certainly contained in the clear contents of vesicles, in the pus of pustules, and in the scabs. It is also present in any secretions or excretions which become mixed with the products of the eruption (exanthem, or enanthem). The blood sometimes seems to contain it.

The virus is extremely resistant to atmospheric influences and to light. It can remain virulent for years, despite drying and exposure to the light, and can then still be used for variolation. The virus also resists disinfectants.

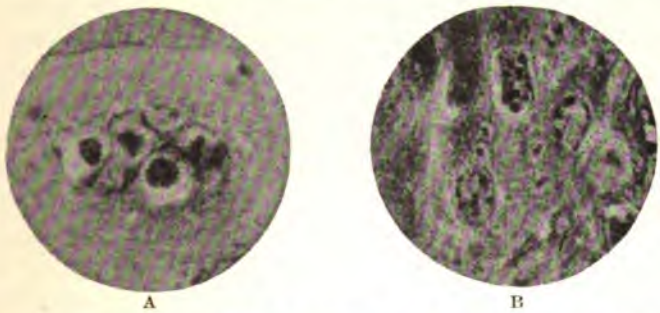
The virus, both of variola and of vaccinia, passes through ordinary filters (Negri), but not through colloid filters (Prowazek).

Since vaccinia is now believed to be a *modified* variola, it seems probable that the microörganisms causing the two conditions must be closely related.

Of the protozoönlike organisms already described in smallpox or in vaccinia may be mentioned (1) the *Monocystis epithelialis* (L. Pfeiffer, 1887); (2) the *Cytorrhyctes variolæ* (Guarnieri, 1892); and (3) the *Chlamydozoan organisms* of Prowazek.

Guarnieri *inoculated the cornea of rabbits* with lymph and studied the disease of the protoplasm of the cells before inflammatory products reached the cornea. After two or three days, he found, in the protoplasm of many epithelial cells, one or two small bodies of variable size, surrounded by a clear zone, the bodies seeming to undergo fission. On examining a scraping of the cornea, he made out, he believed, ameboid movements of these bodies. They remain in the protoplasm, outside the nucleus, and are generally known in the literature as **Guarnieri's corpuscles.**

Pfeiffer believes that Guarnieri's corpuscles represent a young stage of the virus, which, in its second stage, develops into a cyst, with spore formation.



A B

Fig. 128.—A—Four Small Vaccine Bodies Situated in the Cytoplasm of Epithelial Cells Situated at a Distance from the Nucleus. Gland Duct of Nasal Mucous Membrane of the Calf. ×1,000. B—Two Vaccine Bodies Indenting the Nucleus of an Epithelial Cell. Vaccination of the Calf's Cornea. ×1,500. (After E. E. Tyzzer, J. Med. Res.)

In the United States, Councilman, Calkins, and Howard look upon Guarnieri's corpuscles as the parasites of smallpox, and the parasite is called the *Cytorrhyctes variolæ* by Councilman, Brinkerhoff, and Tyzzer, while, in France, Metchnikoff

regards them simply as cell derivatives. One thing seems certain: they are specific appearances in variola and in vaccinia. Since they occur constantly in these two conditions, and are absent under all other conditions, they are of considerable practical significance for differential diagnosis. (For the technic of the corneal experiments, see the articles of Hueckel and of Wasielewski.)

According to Prowazek, though the virus of variola (and of vaccinia) passes through an ordinary filter, it does not pass through a colloid filter; hence it can be first separated from ordinary bacteria by an ordinary filter, after which the filtrate can be put into a colloid filter; the residue on the surface of the filter containing the virus is found to consist of minute, stainable, coccuslike structures, which multiply by subdivision. These, when inoculated into a rabbit's cornea, give rise to Guarnieri's corpuscles; Prowazek, therefore, regards them as the cause of the disease. He distinguishes *elementary* corpuscles ($\frac{1}{4}$ μ in size), which arise from so-called *initial bodies* ($\frac{1}{2}$ μ in size). These latter are formed in the protoplasm of the epithelial cells of the cornea, and from them Guarnieri's corpuscles develop, as reaction-products of the epithelial cells. Inclosed in the Guarnieri bodies, the initial bodies undergo subdivision to form the small elementary corpuscles, which, in turn, can produce the infection in man, or in other animals. They belong to the *Chlamydozoa*.

In addition to the protozoan infection, smallpox is dependent, in the suppurative stage, upon the activity also of the staphylococci and the streptococci, in the pustules. These pyogenic cocci are often present, also, in the blood, so that in the suppurative period we have to deal with a *mixed infection* of the virus proper with a pyogenic infection. The condition is not unlike scarlet fever, in which the infection due to the virus proper may be combined with streptococcus infection.

Epidemiology.—The virus is spread through *fomites* (linen, clothing, utensils) that have been in contact with the patient. It is also spread by *third persons* (physicians, nurses, relatives, and other contacts), the virus apparently being carried by the skin, hair and clothes. As regards indirect contact, it seems likely that third persons may infect *fomites*. Again, *dust and droplet infection* play a part, and apparently the virus can be carried for some distance through the *air*—100 meters (Immermann), 2 miles in the direction of the prevailing wind (Tresh). It is possible that *insects*, especially flies, may help to distribute the virus. Third persons, owing to the extraordinary tenacity of the virus, may carry it hundreds of miles from the patient, remaining healthy themselves, and set up the disease in others. Similarly, contaminated *fomites* may be carried long distances without injury to the virus; thus, the cases occurring in Vienna in 1907 were probably started by contaminated goose-feathers coming from Russia and Poland (Mairinger).

The main **portal of entry** must be the mucous membrane of the respiratory tract, since the virus is usually taken in with the inspired air. The possibility of infection through the digestive tract and through the skin must be admitted.

According to von Pirquet, the virus, multiplying during the incubation period, gives rise to antibodies, which, uniting with the antigen in the skin, cause the exanthem.

Susceptibility.—Most human beings, not all, are susceptible at any age. Pregnant women seem to be especially susceptible. As to races, blacks seem to be highly predisposed. The disease may occur along with other infectious processes (diphtheria, chickenpox, whooping-cough, malaria).

Immunity.—One attack usually yields immunity for the rest of life, but cases of two and of even more attacks are on record. The active immunity does not seem to be a blood immunity but rather an immunity of the cells of the epidermis.

Contagiousness; Incubation Period; Mortality.—The disease is contagious at all stages, from the incubation period until after the crusts have fallen; the most dangerous period is that of the exanthem.

The duration of the **incubation period** is variously estimated at from 1 to 13 days. The period is shorter in variola inoculata.

The severity of the disease varies considerably in different epidemics. The **mortality** before vaccination was introduced was enormous; from 7-10 per cent of all deaths were due to smallpox. The death rate in unvaccinated persons ranges from 25-35 per cent (Osler). There is still far too much smallpox in the United States and Canada, due to neglect of vaccination, and the absurd fanaticism of antivaccinationists. We still have from 25,000 to 30,000 cases per year in the United States alone!

Symptoms.—The incubation period is followed by: (1) The INITIAL STAGE, beginning with the appearance of the fever and ending with the appearance of the exanthem. (2) The ERUPTIVE STAGE, during which the *exanthem*, beginning on the scalp and face, passes gradually downward over the body and is associated with a marked *remission of the temperature* at the same time, the *enanthem* appears on the mucous membrane of the mouth and throat. This stage lasts until the first vesicles appear in the middle of some of the papules. (3) The FLORID STAGE. This begins with the *vesiculation* of the papules and ends when the vesicles begin to change to pustules; it is accompanied by a moderate elevation of temperature and by enlargement of the single skin lesions. (4) The STAGE OF SUPPURATION. During this stage the contents of the *vesicles become purulent*. It is the most dangerous stage. The fever is remittent, corresponding to the suppuration. (5) The STAGE OF DESICCATION. The pustules now begin to *dry* up; the temperature falls by lysis. (6) The STAGE OF DECRUSTATION. As a result of the desiccation, *scabs* are formed on the surface and the defects in the epidermis and corium underneath gradually heal, leaving pigmented areas or *scars* behind.

The typical form of smallpox is the so-called (1) *variola discreta*. Less common forms are: (2) *variola confluens*, in which the single efflorescences appear in such large numbers that they fuse with one another; (3) *varioloid*, in which the number of efflorescences is very scanty and the inflammatory phenomena in the suppurative stage slight; (4) *variola sine eruptione*, very mild cases in which no exanthem occurs at all, the

A

B

Fig. 129.—The Exanthem of Smallpox. (Med. Service, J. H. H.)

whole disease being completed at the end of the initial stage; (5) *variola hemorrhagica,* in which, owing to the presence of a hemorrhagic diathesis, hemorrhages occur into the vesicles and pustules, giving rise to so-called "black" smallpox; (6) *purpura variolosa,* an absolutely fatal form, in which an acute hemorrhagic diathesis develops suddenly, with high fever, due to the smallpox virus, and death occurs before any exanthem appears; and (7) *variola inoculata,* due to inoculation of smallpox virus, and taking a peculiar clinical course.

(*a*) *Variola discreta*

At the end of the incubation period, the patient begins to feel chilly, and may have an actual rigor, the temperature rising in a few hours to 103° or 104° F., and remaining at this level for 3 days, with slight morning remissions. The patient complains of severe headache, dizziness, and anorexia, but the most important symptom of this initial stage is the *severe pain in the lumbosacral region.* During this period, a *prodromal exanthem* appears in many of the cases. It may take either one of two forms: (a) a *macular rash* of pale rose or dark rose color, the macules varying in size from that of a pea to that of a thumb-nail, sometimes fusing with one another to form large diffuse reddened areas. This rash is sometimes spoken of as the "measly" form, but in reality it does not closely resemble the measles exanthem, the central, dark, slightly raised part of the measles efflorescence not being present. This type of rash usually appears on the second day of the fever and is most often seen on the face, and on the extensor surfaces of the limbs, less often on the trunk. It lasts only a few hours, as a rule, though it has been known to continue for a couple of days. It is often overlooked.

(b) The second or *scarlatiniform initial exanthem* is much more local in its distribution, being usually situated in the so-called SIMON'S FEMORAL TRIANGLE, the base of which is formed by a line connecting the two anterior superior iliac spines with one another, and the sides by lines connecting these points with a point lying between the knees when the thighs are completely adducted. The triangle, accordingly, includes the skin of the lower abdomen, and that of the anterior and medial surfaces of the thighs. This exanthem usually appears on the first day of the fever (earlier than the *rash* above described). It takes the form of a diffuse, even discoloration of the skin, of a red color, often with a cyanotic cast. This exanthem so closely resembles that seen in scarlet fever that it is sometimes called the "scarlatiniform" exanthem. In its area, petechiae may occur. Occasionally, this form of exanthem is met with on the lateral surface of the trunk; in other instances, it is seen on the lateral region of the thorax, or on the medial and anterior surfaces of the upper arms ("shoulder triangle").

'he initial exanthemata are more abundant in some epidemics than hers.

he Initial Stage.—This is ushered in with fever, headache, and severe in the back, in which the above described initial exanthems may ır; it lasts about 3 days.

he Eruptive Stage.—On the face, on the hairy scalp, and on the upper of the chest, the typical exanthem now begins to appear. At the

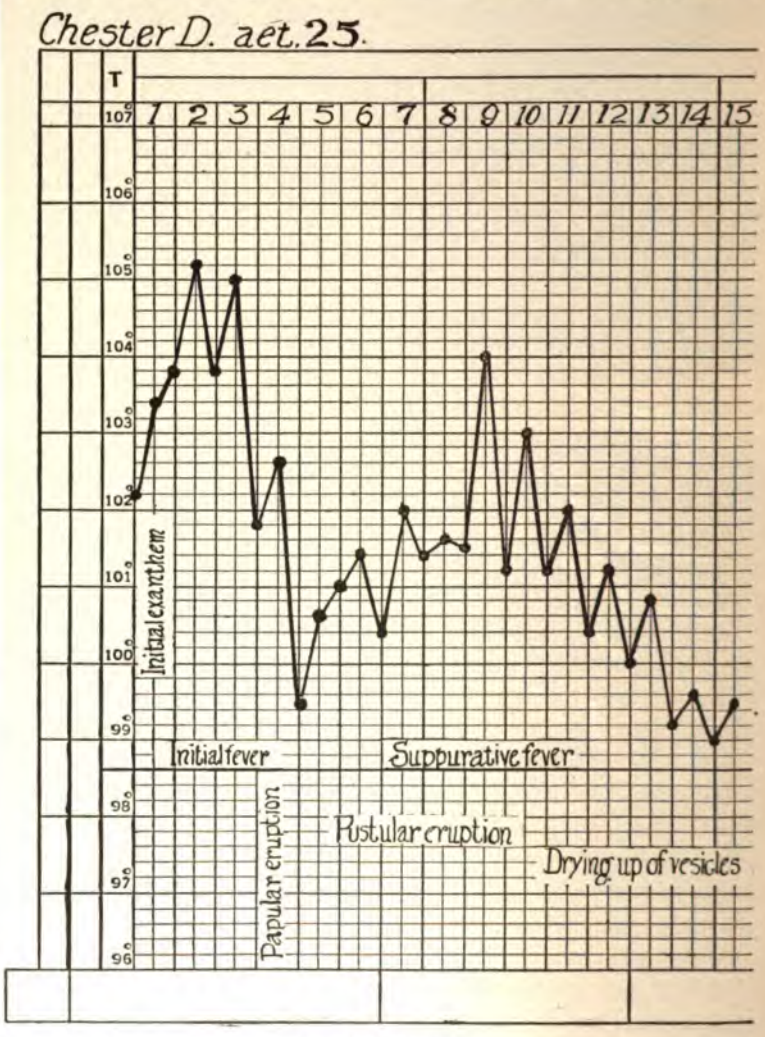


Fig. 130.—Variola.

time, there is a marked remission in the temperature, the headache pains in the back become much less, the patient feels very much r, and may think that he is getting well. He breaks out into a pro-

fuse sweat, and may himself attribute the beginning eruption to the sweating. During the 3 days of this stage, the temperature gradually falls to normal. On examining the exanthem, it is found to consist of single papules, elevated a little above the level of the skin; these are of the size of a small pin's head, and are, ordinarily, about 1 cm. apart at first, though they rapidly increase in size, and become of a deeper red color, during the 2 or 3 days following their appearance. By the sixth day of the disease, they are of the size of peas, and are palpable, as firm nodules. The exanthem gradually *spreads from above downward,* lesions being most numerous on the face and scantiest on the feet. Areas of the skin in which the scarlatinal initial rash was present are often relatively free from the exanthem. The exanthem, however, involves practically the whole skin of the body, the individual lesions being more advanced headward, and progressively less advanced as the feet are approached.

Contemporaneous with the exanthem, an *enanthem* appears in the mouth and throat; it can be seen also in the mucous membrane of the nose, in the conjunctiva, in the vagina, and in the rectum.

The Florid Stage.—This begins when the papules on the face begin to become vesicular. In the most prominent part of the papule, now about the size of a pea, a minute glistening *vesicle* appears. This vesicle gradually enlarges, and becomes distended with serum; it rests upon a *tough, infiltrated base,* this in turn being surrounded by a narrow red *halo.* The vesicle has a characteristic gray color, and looks opalescent, reminding one of mother-of-pearl. Each vesicle is subdivided by septa, so that, to empty it, several pricks at the circumference are required to release the clear contents (*variola lymph*). About 2 days are required to complete the transformation of the papules into vesicles in this florid stage. The temperature remains low.

Similar changes take place in the enanthem, and cause subjective discomfort. Here, however, the vesicles often rupture, leaving erosions, or shallow ulcers, behind. There is salivation, dysphagia, hoarseness, nasal obstruction, and pain on urination and on defecation.

Stage of Suppuration.—The florid stage changes at the end of 2 or at most 3 days into the dangerous suppurative, or maturative, stage (end of the first, or beginning of the second, week of the disease). The temperature again rises. This is the most dreadful stage for the patient, as his sufferings become intense, owing to the painful skin and mucous membranes, the intense itching, and the burning of the eyes. The vesicles become filled with pus, the halo about each pustule enlarges, and, where the pustules are close together, the skin becomes diffusely red and swollen from inflammatory edema. The patient can scarcely open his eyes, owing to the swelling, and the whole face becomes a caricature, scarcely recognizable. As the vesicles become purulent, or even earlier,

many of them show umbilication. The purulent change begins in the vesicles of the face and head, and gradually extends downward, as did the original eruption. The ulcers in the mouth excrete pus. The breath becomes extremely fetid. The cough becomes more troublesome, the respiration noisy. The patient gives off, at this period, the typical specific penetrating smallpox odor.

The temperature chart shows a steplike rise of the fever-curve. Sometimes the patient becomes dull and delirious. The pulse is accelerated, of low tension, and often arhythmic.

By the middle of the second week, some of the pustules begin to break, the suppuration continues, the fever remaining high and remittent, until, by the end of the second week, the process begins to ameliorate and desiccation and crust formation follow.

Stage of Desiccation.—This stage, like the other stages, begins in the face, the diffuse inflammatory process diminishes, the temperature gradually falls by lysis, and the pustules dry up, with the formation of brownish, rough-looking scabs. As the hyperemia diminishes, the infiltration at the base of the single pustules grows less. By the end of the third week, the desiccation has involved all of the lesions, as far as the feet. The enanthem undergoes simultaneous regressive changes, as the temperature gradually falls to normal. The patients begin to sleep better, and the appetite improves. During the desiccation, pruritus is usually marked, and the patients have to be warned against scratching.

Stage of Decrustation.—At the end of the third week the scabs begin to loosen and to fall off, leaving brownish, pigmented areas or scars behind. The number of scars depends upon the extent of the involvement of the corium. These scars persist through life. They are most numerous on the face. In some patients, locks of hair fall out; fortunately, it grows in again, if the lesions are not too deep. The stages of desiccation and decrustation occupy a period of 2 or 3 weeks, and the patients, during this period, improve in every way, though the muscular weakness may be very marked. The total duration of the disease, in uncomplicated cases ending in cure, amounts, therefore, to 4 or 5 weeks.

Papules on the palms of the hand and soles of the feet may, on account of the thickness of the superficial epithelium, never form pustules on the surface. The products of these deep-lying lesions are therefore not cast off by decrustation, but must be slowly absorbed, a process often taking months. During this time the appearance of the round, mahogany-colored, or brown spots in the skin of the palms and soles is diagnostic of the past attack of smallpox.

The **blood** in smallpox has been studied especially by Kammerer. The white cell count is increased in the florid stage (10,000 to 20,000 W. B. C.), but it gradually decreases afterward. The increased number of white cells is due chiefly to an absolute increase in the lymphocytes, and a

relative lymphocytosis can be made out for as long as 3 months after the attack. The polymorphonuclear neutrophils are relatively diminished, though their absolute numbers may be normal, or slightly increased. In the severer cases, a small number of myelocytes and of normoblasts may appear in the blood. The large mononuclears and transitionals seem to be unchanged, and no marked alterations in the number of eosinophils and of polymorphonuclear basophils have been made out. It is surprising that there is not a great increase in polymorphonuclear neutrophils during the suppuration stage.

These blood findings may be of some help in differential diagnosis, since, as we have seen, there is an outspoken leukopenia in measles, and an outspoken eosinophilia in scarlet fever. Unfortunately, the blood-findings are not of much help in distinguishing chickenpox from smallpox.

Mortality.—The death rate in variola discreta varies in different epidemics, but usually is between 15 and 25 per cent.

(*b*) *Variola confluens*

This is the severest of the purely pustular forms of smallpox; most of the cases die. This type gets its name from the fact that the single lesions fuse together in the suppurative stage, owing to their large number. All the subjective symptoms of every stage are exaggerated. There is, of course, every degree of transition between variola discreta and variola confluens. The several stages are usually shorter than in variola discreta, the whole process running its course more quickly; sometimes the whole face looks as though it were a single vesicle or pustule ("parchment mask").

In these cases, the heart muscle is often severely injured, and death is frequently due to myocardial insufficiency. Hyperpyrexia is frequently seen. Occasionally, a patient recovers, with deep disfigurement (scars, loss of hair, corneal turbidities, and ectropion).

(*c*) *Varioloid*

In so-called varioloid, the exanthem is scanty and the suppurative stage mild. Many of these patients recover without any scarring. In the initial stage, patients suffering from varioloid are more apt to have the "rash" than the "scarlatiniform exanthem." All the stages are shortened. The enanthem is usually slight. The single efflorescences are smaller, and more delicate, than in variola discreta.

This is the form of smallpox that we most often see nowadays, owing chiefly to the prevalence of vaccination. The cases are often incorrectly diagnosed owing to their mildness, but the skilled observer, who carefully considers the anamnesis and the course of the disease, especially

the developmental process from the smallest papule to the single pustules, will scarcely fall into error. When a chickenpox case is not seen until its late stages, and an anamnesis is not obtainable, differentiation may not be possible without inoculation of a rabbit's cornea.

(*d*) *Variola sine eruptione*

The initial stage is like that of variola discreta. The initial rash may be present, but the eruptive stage does not appear. In order to make a diagnosis, the possibility of infection, the determination of the incubation period, and the exclusion of other causes for the fever are necessary. Cases of smallpox without exanthem are certainly not uncommon; they are probably more numerous than we realize, and are doubtless responsible, when they go unrecognized, for the spread of the disease. Many of these patients continue ambulatory. The whole process is mild, and there is no mortality.

(*e*) *Variola hemorrhagica*

(*Variola pustulosa hemorrhagica, Black Smallpox*)

This form is characterized by its complication with a hemorrhagic diathesis. It occurs most often in older people who are run down, and is common in alcoholics and in the cachectic.

The initial stage is severe (high fever, severe pains in the back). The eruptive stage lasts longer; indeed, the whole course of the disease is prolonged. The hemorrhages may begin to appear during the stage of eruption, or in the florid stage, though they are most common in the suppurative stage. The temperature as a rule is not high during the suppurative stage. The lesions as a result of the hemorrhages turn bluish-black in color. The skin between the lesions is pale. It is interesting that the hemorrhages begin in the pocks of the lower extremities and gradually extend upward, contrary to the general rule regarding the different stages of the eruption in smallpox. Hemorrhages in the skin, between the pustules, sometimes occur. They may also occur in the mucous membranes.

Most of these cases are fatal. Should recovery occur, convalescence is protracted.

(*f*) *Purpura variolosa*

This form is invariably fatal. Young, strong persons of both sexes, and pregnant women, are most frequently victims. The eruptive stage does not appear, the severe hemorrhagic diathesis developing in the initial stage, and causing death before the outbreak of the exanthem.

Concerning the etiology, there can, however, be no doubt, since the disease is contracted from patients showing the pustular form, and a patient suffering from it may lead to the infection of others in whom typical pustular forms develop.

The incubation stage is shortened. The initial symptoms are violent. On the first or second day of fever, a diffuse scarlatiniform erythema, with pin-head-sized cutaneous hemorrhages, develops all over the body. The hemorrhages spread rapidly; in the face, they often follow the folds of the skin, giving rise to bluish-black streaks. The eyelids become black and blue from the extravasations, and blood oozes from the mouth and nose. There are often, also, hemorrhages from the mucous membranes (lungs, intestine, stomach, bladder). Death occurs between the third and the fifth day.

(*g*) *Variola inoculata*

This is now seldom seen, but, before the introduction of vaccination, was known to every physician. It may occasionally occur accidentally, through inoculation of the skin of a "contact."

After an incubation period of 3 or 4 days, a small papule appears at the site of inoculation, and gradually increases in size and in elevation; next, a small vesicle appears in the papule and gradually enlarges; its contents are at first clear. On the sixth or seventh day, a marked areola develops around the vesicle, and its contents become purulent. The temperature rises, and the general phenomena may be severe. After 3 days of this, the temperature falls, the subjective symptoms lessen, and a general eruption, corresponding entirely to that of ordinary variola discreta, appears, its severity corresponding to the number of lesions. The course is usually that of varioloid.

The main differences between variola inoculata and variola discreta are: (1) the shortening of the incubation period to 7 days, and (2) the divisibility of the whole course into two parts: (a) local phenomena, during the first 7 days, (b) generalized exanthem, afterward.

Complications of Smallpox.—These include (1) pyemic metastases, (2) erysipelas, (3) local phlegmons, (4) suppurative buboes in regional lymph glands, (5) bronchitis and bronchopneumonia, (6) pleuritis, (7) myocardial insufficiency, (8) polyarthritis, (9) encephalitis and myelitis, (10) polyneuritis, (11) otitis media, (12) keratitis with perforation, iritis, and panophthalmitis.

Diagnosis.—This should not be difficult, if what has been said regarding the symptoms and the whole course of the disease be attentively considered. We first consider whether we have to deal with a universal exanthem, or with a local eruption. If it be *local*, variola can be excluded and the disease will probably turn out to be acne, eczema, herpes, furunculosis, prurigo, impetigo contagiosa, or some similar eruption. Among the *universal* exanthematous diseases we have to distinguish smallpox (1) from *measles* (higher fever in the papular stage, Koplik's spots); (2) from *rubeola* (macules, not papules, simultaneous appearance all over the body rather than spread from above downward); (3) from *scarlet fever* (severer angina, pallor about the mouth, fever highest when the exanthem appears); (4) from *typhus* and *typhoid fever* (no fall of temperature with the exanthem; blood culture in typhoid); (5) from *varicella* (typical large, watery, clear vesicles, surrounded by narrow red zone appearing within a few hours, without marked infiltration of the base).

When there is the least doubt about the diagnosis, the patient should be treated as a case of smallpox until a decision has been arrived at. Whenever necessary, the corneal experiment should be resorted to to settle the diagnosis.

If the patient suspected to be coming down with smallpox has not been vaccinated, he should be vaccinated at once. If this be done in what looks like a florid stage, or a suppurative stage, and is followed by a typical vaccination lesion, variola can be excluded.

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7. Vaccinia (Cowpox and Vaccination)

The nature of this disease of cattle has been described above in connection with smallpox.

The lymph from the vaccinia vesicles is used as a vaccine to protect human beings from smallpox.

Vaccine virus is usually obtained from calves suffering from cowpox, though men, monkeys, guinea-pigs, rabbits, rats, camels and many other animals are susceptible, and lymph from the lesions produced in them has, also, sometimes been used for vaccination.

Formerly, vaccine virus obtained from human beings was much employed, but since bovine virus can be purified by glycerin (Copeman), the use of the latter has become almost universal, and the danger of syphilitic infection attendant upon the use of human virus is excluded.

Formerly, dry splinters of ivory, coated with vaccine-lymph, were employed in vaccinating. Now the virus is first treated with glycerin for a time (glycerinated lymph); this kills ordinary bacteria but preserves the active principle of the vaccine virus, provided the glycerin has not acted too long upon it (not over 6 weeks in summer, or 3 months in winter). Vaccine virus, even when glycerinated, always contains bacteria, but when the virus is properly prepared, they are non-pathogenic for man.

Definition of Vaccination.—By this is meant the transmission of cowpox (vaccinia) to man by inoculation, for the purpose of conferring on him a temporary immunity against smallpox (variola).

Historical.—In May, 1796, Edward Jenner took some of the lymph from a pustule in a milkmaid who had accidentally inoculated herself with "original" cowpox, and inoculated an eight year old boy with it. The boy developed vaccinia and recovered. Jenner then inoculated him with smallpox virus. The boy did not develop variola inoculata but remained healthy. During the following two years, Jenner made several such tests on different persons with the same result, and in 1798 published his celebrated article in which he advised the general adoption of vaccination with cowpox as a prophylactic measure against smallpox. This was one of the greatest discoveries ever made by a medical man.

Technic.—Vaccination is a slight surgical operation, which should be aseptically performed. Formerly, vaccination was done by scarification or by scratching. This method is now prohibited by law in Germany, as it invites infection (pyogenic cocci, tetanus bacilli). The best method

of vaccination is by *incisions* with the point of a scalpel, or of a sharp, flat needle. The incisions should *not be deep enough to draw blood,* though the line of the cut may be blood-tinged; if a drop of blood appears, it does no harm. Three or four incisions, parallel to the long axis of the arm, 2 cm. apart, each incision being 1 cm. long, are best. The site usually chosen is the lateral part of the skin on the upper right arm; in re-vaccination, the left arm is used. In young women, the front of the thigh may be selected instead of the arm; it is unwise to vaccinate little girls on the thigh. The glycerinated virus is then placed upon the area incised, and is gently rubbed in with the flat side of the knife, or of the needle, any unnecessary irritation being avoided.

Simple preparation of the skin (scrubbing with soap and water, followed by alcohol and *thorough drying*) is enough. Antiseptics should not be used, as they may kill the virus. The skin should be *perfectly dry* before incision. The incisions are perhaps best made with a sharp needle, since it can be easily sterilized by passage through a flame.

After applying the vaccine, the arm should be allowed to dry in the air for 15 minutes. No dressing is required. An important exception is made in children, or in adults who are suffering from any skin-lesion (eczema, prurigo, pemphigus, etc.), for in them, through scratching, the cutaneous lesions may be infected with vaccine virus, a serious complication. In such instances, the vaccination site should be covered with a sterile gauze dressing (free from all disinfectant substances). Shields are unnecessary and are often harmful. The person vaccinated and the family should be instructed regarding the possibility of transferring virus from the inoculation site to the eyes, to small wounds or eruptions, or to rhagades, on their own bodies, or on the bodies of others, by the fingers (scratching). Mairinger reports an instance of a child who, bathing in the same bath-water as that used by a child just vaccinated, was extensively inoculated over the face and trunk.

A 4 per cent alcoholic solution of picric acid is applied to the vaccinated area 48 hours after vaccination by Schamberg and Kolmer. It is said to lessen the local reaction, and to diminish the danger of bacterial infection. This precaution has not, as yet, been widely applied. During the scabbing stage, a dusting powder composed of dermatol 10.0, zinc oxide 10.0, starch 40.0, and talcum 40.0 is recommended by Paul.

Symptoms Following Vaccination.—Except for slight traumatic reaction, nothing is visible for 3 or 4 days (*period of incubation*). If the vaccination "takes," *papules* begin to appear on the skin at the sites of incision, usually on the 3d day. They are round, or oval, firm papules, v. Pirquet's "papilla," of a bright red color; they gradually grow more prominent, and are surrounded, up to the 7th day, by a narrow light red zone, the aula, *halo*, or inner areola. On the 5th or 6th day, a *vesicle* appears at the summit of the papule. This enlarges, becomes distended

with fluid, looks pearl-gray, is umbilicated, and is, at its base, surrounded by a swollen red areola—THE JENNERIAN VESICLE—resembling a "pearl upon a rose leaf." The full development is reached by the 7th or 8th day. The central umbilication is marked; the second red zone, or *outer areola*, has formed (outside the aula). Von Pirquet regards the outer areola as the most striking and characteristic phenomenon of the vaccinia lesion. A day later, that is, at the beginning of the 2d week, the STAGE OF SUPPURATION begins. The vesicle turns yellowish, and the so-called *second umbilication* appears, the outer areola widens, and its flaming red color deepens, the perivesicular swelling increasing.

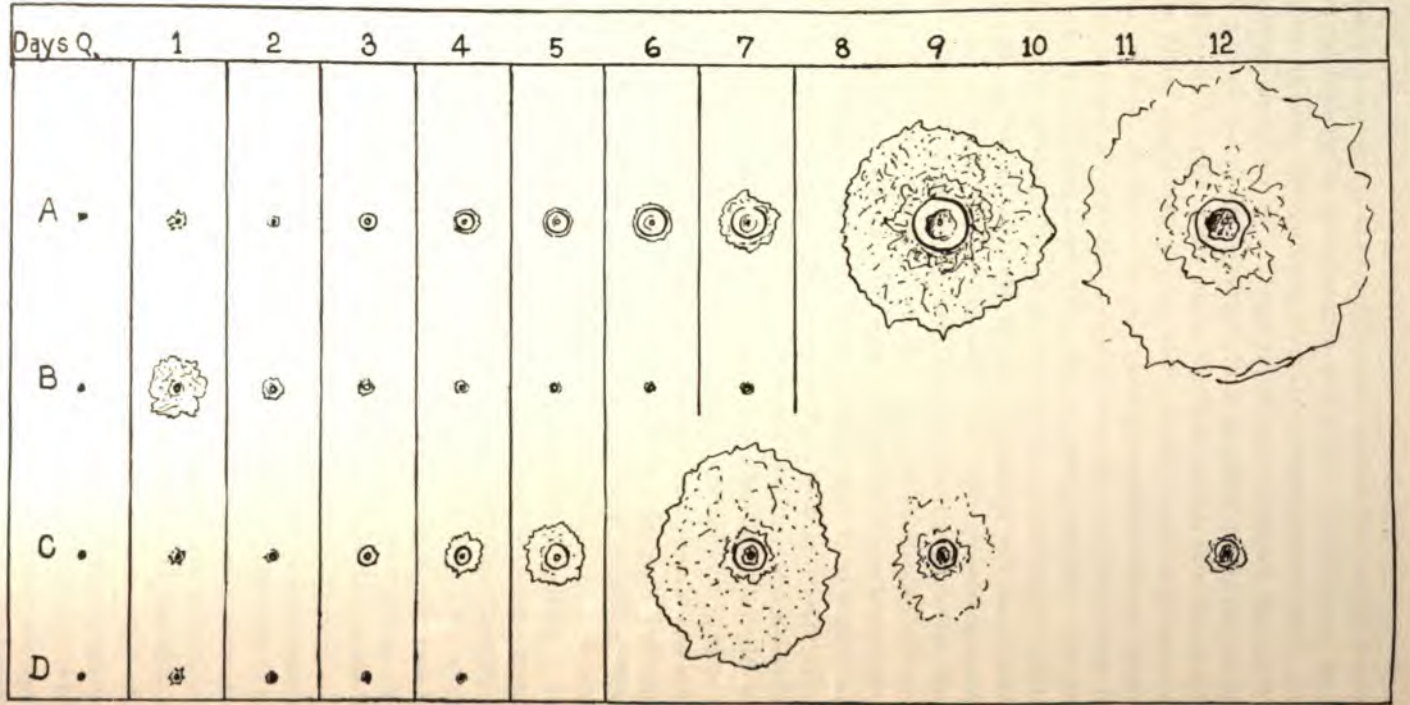
The arm may now be quite painful. By the 11th day, the distended yellow pustules stand out prominently on the bright red, erysipelaslike areolar plateau; at the periphery of the plateau, however, the redness goes over very gradually into the color of the normal skin, in marked contrast with the sharply circumscribed hyperemia of erysipelas. Palpation of the axilla reveals *enlarged and tender lymph glands*. By the 11th day, the redness and swelling begin to go down, and the STAGE OF DESICCATION begins. Two or 3 days later, the vesicle dries up, and by the end of 1½-2 weeks, a brown, wrinkled SCAB is left, which should be allowed to drop off from itself, in order that the healing process may go on, undisturbed, beneath it. The reddish scar, later, turns white, and remains as a characteristic "VACCINATION MARK."

There are often slight constitutional symptoms, at the beginning of the suppuration, including fever. The fever is of variable height; the curve shows a steplike ascent; the temperature falls by crisis when desiccation begins.

Between the 7th and the 14th day, there is sometimes a very *transitory universal exanthem*, consisting of small roseolar macules, much like the "morbilliform initial rash" of variola. More often, at the acme, a few *accessory* pock-lesions appear near the inoculation site. Rarely, a *generalized vaccinia* develops, small pustules breaking out all over the body at the acme, on the 9th or 11th day, soon drying up to small crusts, and leaving no scars. One of my own children had such a generalized vaccinia.

The LEUKOCYTE COUNT, as followed by Sobotka, undergoes strange changes. On the 3rd or 4th day after vaccination, there is an *initial leukocytosis*, which continues until the 7th or 8th day; the count then falls to normal and lower (*leukopenia*), continuing until the 10th or 12th day, to be followed by a *terminal leukocytosis*, lasting 2-3 days. In the patients who become more ill, and in whom nasty-looking sores develop, a complicating pyogenic infection is probable.

Successful vaccination yields IMMUNITY AGAINST SMALLPOX as soon as the Jennerian vesicle has developed, and also, for a considerable length of time, against vaccinia itself. The nature of the immunity is unknown.



121.—Effects of Cowpox Vaccination in Man Watched from Day to Day: A, First Vaccination with Cowpox. B, Re-vaccination After a Short ; Early Reaction. C, Re-vaccination After a Long Interval. D, Traumatism Alone. (After C. E. von Pirquet, Arch. Int. Med.)

The duration of the immunity against variola from a single vaccination is temporary, not permanent, the duration varying in different persons. On the average, the vaccinated person is well protected against accidental variola infection for about 10 years, though the period of protection against variola inoculata by vaccination is shorter than this.

Every child should be successfully vaccinated during its first year (before the second summer), and, again, about the tenth year. If the first vaccination be not successful, not "taking" at all, or yielding only a rudimentary result, it should be repeated. Should the second vaccination with reliable vaccine prove negative, the existence of some natural immunity may be assumed. On exposure to smallpox, it is well to *re-vaccinate,* at once, unless the patient is known to be immune, or has been successfully vaccinated a very short time before. Vaccination at the beginning of the incubation period of variola will either completely protect, or protect enough so that only varioloid will develop.

The reactions on RE-VACCINATION have been carefully studied by von Pirquet and have thrown much light upon the phenomena of anaphylaxis (allergy). Anyone interested in the variable phenomena of re-vaccination should consult his admirable monograph.

Dangers of Vaccination.—Vaccinia is an acute infectious disease. Moreover, during vaccination, an open wound is produced, which, if the work be not done aseptically or the lymph be bad, may become infected ("early infection"); "late infections," when they occur, are usually due to improper care of the arm, or to scratching.

When vaccination is performed, with good lymph, and proper instructions regarding cleanliness and care during the course of the reaction are followed, the dangers are minimal and the benefit conferred enormous.

In *hemophilia,* if vaccination be done at all, the greatest caution should be observed.

In patients with *leukemia* very severe local reactions have been observed.

The danger of *auto-inoculation* and *hetero-inoculation* of the eyes and of skin lesions has already been referred to.

Complications.—Wound-infection from pyogenic cocci, or from tetanus bacilli, may occasionally occur. These are best avoided by using pure glycerinated lymph, and by vaccinating by incision instead of by scarification, since glycerin, of itself, may not kill the spores of tetanus. All vaccine virus is especially tested for tetanus before being placed on sale. In the days when human lymph was used, the possibility of the transmission of syphilis was much discussed; the use of animal lymph excludes this possibility.

Vaccine virus is believed to be a modified form of smallpox virus (see Smallpox). It is possible that the cause of smallpox is the parasite *Cytorrhyctes variolæ,* described by Councilman, Brinkerhoff and Tyzzer. This parasite appears

to have a sexual and an asexual cycle. According to Calkins, smallpox is caused by the combined asexual and sexual cycle of the same parasite, the sexual cycle occurring in a nucleus of the epithelial cell. If the parasite loses its power to generate by sexual division (as in cowpox), it can never regain it. Thus while smallpox may be modified into cowpox, cowpox can never be changed back to smallpox again. Though this view has not yet been generally adopted, it is suggestive and interesting.

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8. Sweating-Sickness

(*Febris miliaris*)

Definition.—Sweating-sickness is a disease formerly prevalent and very fatal in England, but now largely confined to France and Italy. It occurs in epidemics in which a large number of persons are attacked within a few days by fever, profuse sweats, and an eruption of miliary vesicles. In the severe cases, there may be delirium, prostration and a hemorrhagic diathesis.

Etiology.—The cause is unknown. The disease is directly contagious, and the virus is probably air-borne. The epidemics occur in spring and in summer. Relapses are common in the first or second week of convalescence.

Diagnosis.—This is difficult to make at the beginning of an epidemic; afterward, it is easy. The early cases are often taken to be measles or scarlet fever.

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9. Rocky Mountain Spotted Fever

Definition.—An acute infection, characterized by chills, fever, pains in the back and bones, and a macular exanthem, which is sometimes hemorrhagic. It occurs especially in Montana (Bitter-root Valley), Idaho, Nevada and Wyoming, in the mountainous districts.

Etiology.—The nature of the virus is unknown, but the disease is undoubtedly transmitted by a tick (*Dermacentor occidentalis*), as shown by King and Ricketts. Wilson and Chowning believed that the disease is due to a piroplasma, but this has not been confirmed. Guinea-pigs and monkeys are susceptible. One attack yields immunity. Immune sera can be produced in guinea-pigs and in horses (Ricketts; Hanemann and Moore).

Symptoms.—The incubation period is from 3 to 10 days. The onset is then sudden with chill, fever and pains over the body. A rash appears on the 2d to the 7th day resembling that of typhus exanthematicus, the macules usually becoming hemorrhagic. Fever of 103°–105° F. develops. Delirium is common. After a course of 3 weeks, convalescence begins. The mortality is variable; it was small in Idaho (3 per cent); high in Montana (70 per cent). The tick that transmits the virus lives upon the bodies of horses and of cattle.

Differential Diagnosis.—The disease must be distinguished (1) from measles; (2) from typhus exanthematicus; (3) from influenza; (4) from dengue; (5) from epidemic cerebrospinal meningitis; and (6) from typhoid.

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B. Non-Exanthematous Diseases

1. Mumps

(*Parotitis epidemica, Ger. Ziegenpeter, Fr. Oreillons, Ital. Orecchioni*)

Definition.—Mumps is a specific, febrile, infectious disease, most often met with in the young; it is extremely contagious, and causes an acute inflammation of one or more of the larger salivary glands, usually the parotid, on one or both sides. It has been known since the time of Hippocrates, who described it carefully and knew of its contagiousness and of the occurrence of a complicating orchitis.

Etiology.—The nature of the virus is unknown. It is probably no ordinary bacillus or coccus, but is more likely a virus like that of the acute exanthemata or like that of the Heine-Medin disease, lyssa, etc. Attempts to reproduce the disease in animals have failed, until recently (1913). Nicolle and Conseil assert that, on intraparotid injection into monkeys of a punctate from the swelling in human mumps, a mild fever, lasting several days, is manifested after an incubation period of 16-26 days; in one of the monkeys, the parotid gland became slightly swollen.

Epidemiology.—The disease is directly contagious from person to person, and the danger of contagion lasts for several weeks. The disease is often met with in epidemics, but sporadic cases also occur. Local epidemics are common, confined to a single institution (orphan asylum, jail, ship, barracks), or even to a single house, or to a single room in a house. The virus can be carried by healthy intermediate persons. It is remarkable that many persons exposed, and presumably susceptible, do not contract the disease. Spread by *fomites* has not been established. The disease is more common in cold wet weather than at other seasons, but it occurs at all times of the year. The spread of the disease seems to correspond more or less closely to that seen in diseases like diphtheria and epidemic meningitis. One attack usually yields permanent immunity, but not always; well-established instances of two, and of several attacks are on record.

Symptoms.—The *incubation period* varies between 14 and 24 days. After 2 or 3 days of fever, headache, diarrhea, anorexia, insomnia, and pain in the neck, a triangular swelling rapidly appears in front of, and beneath, one or both ears, and pain is felt on opening the mouth, on chewing and on swallowing. Sometimes, the swelling of the gland occurs unheralded by prodromata.

The *fever* is intermittent, or remittent, and lasts only 3-4 days, as a rule, and is not high; it falls by lysis. Should the disease process extend to other salivary glands, or should complications, like orchitis, set in, the fever returns.

The disease is most often *bilateral,* though one gland swells usually before the other, the left gland swelling first, as a rule. The inflammatory process involves also the periglandular tissues, so that the whole cheek from the ear down to the margin of the mandible, and behind as far as the mastoid, looks swollen; sometimes the whole face is so markedly swollen that the person is almost unrecognizable; the face is a huge pyramidal "lump," covered by *white* tense skin. The ears stand out from the head and give the patient a comical facial expression, or one suggestive of imbecility (hence the German names *Ziegenpeter* and *Bauernwetzel.* Occasionally the other salivary glands are inflamed also, and the lacrimal glands may be involved. Salivation or suppression of salivary secretion may occur. When all the salivary glands are swollen, together with the tissues about them, the head and neck assume the shape of a huge pear! The neck may be greater in circumference than the head.

The head is held in typical attitudes. In the unilateral affection, the muscles on the diseased side are relaxed and the head is turned toward the swollen parotid; in the bilateral affection, the head is held straight and rigidly, and the face looks anxious. There is stomatitis and *fœtor ex ore.*

The *blood,* as a rule, shows no leukocytosis; in some cases, however, an outspoken leukocytosis has been met with (16,000; 50,000). There is a relative increase in the mononuclear elements.

Relapses are not uncommon.

About a week after the glands have begun to swell, the swelling goes down without suppuration, and no residua are left. In adults, ORCHITIS is not uncommon (oöphoritis is less common); in rare cases, it may be the only sign of the disease. The testicle becomes swollen, tender and hot; hydrocele often develops. The right testicle is twice as often affected as the left. The inflammation usually subsides in from 3 to 7 days. Orchitis is rare in children. In about half the cases of orchitis, *atrophy* of the testicle follows, but sexual power remains; in *bilateral orchitis* followed by atrophy, the patient is sterile. Epididymitis rarely occurs.

Mumps may affect the submaxillary or the sublingual gland alone. Hegler has described an epidemic of SUBLINGUAL MUMPS (*sialoadenitis sublingualis acuta epidemica*) among the Sisters of the Eppendorfer

Hospital in Hamburg. Other occasional complications include (1) pancreatitis, (2) meningitis (always benign), (3) mastitis, (4) otitis, (5) endocarditis, (6) polyarthritis, and (7) iritis.

Diagnosis.—This is easy when an epidemic prevails. Sporadic cases must be distinguished (1) from *toxic parotitis* (due to mercury, lead, or iodin); (2) from *secondary* and *infectious parotitis,* associated with infections elsewhere in the body, and including "post-operative parotitis"; (3) from *ascending parotitis* (due to oral sepsis); (4) from *lymphadenitis;* (5) from *osteomyelitis;* (6) from *periostitis;* (7) from *tonsillitis;* (8) from *parulis* (subperiosteal abscess of jaw, following abscess at the root of a tooth); (9) from *syphilis* of the parotid (gumma); and (10) from *tumors* of the parotid.

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SECTION III

SPECIAL DIAGNOSIS OF DISEASES DUE TO EXTERNAL PHYSICAL CAUSES

Among the diseases to be considered under this heading are:

(A) Those due to long exposure to high temperatures (caloric diseases).

(B) Those due to exposure to cold.

(C) Those due to electrical injury.

(D) Those due to injury from x-rays and radium.

(E) Those due to alterations in atmospheric pressure.

(F) Those due to unaccustomed movements, or to alterations of the direction of movement, of the body (e. g., sea-sickness, car-sickness).

A. Diseases Due to Heat (The Caloric Diseases)

Occurrence.—Aside from the local effects of heat (burns, scalds), human beings may show disease symptoms following the long-continued effect of high temperature. It has been customary to distinguish three main types of the caloric diseases: (1) sun-stroke, or insolation, resulting from exposure of the head to the sun's rays; (2) heat-stroke, or hyperthermia, due to a general overheating of the whole body by conducted heat; and (3) the so-called warmth-stroke, or ignisation, the hyperthermia produced by artificial sources of heat. But there is no real difference between sun-stroke and heat-stroke, and the effect of radiated heat and conducted heat seem to be the same.

Direct exposure to the sun's rays is, however, the commonest cause of the caloric diseases. It has been shown that such direct exposure, even when the temperature of the air is relatively low, causes a much quicker rise of body temperature than hotter air without direct exposure to the sun (Rubner). Heat production through work (as in soldiers on the march), and hindrance to heat dissipation in still air and when the humidity is high, are accessory, but not essential causes. Cases described as "heat-stroke without exposure to the sun" are often, in reality, instances of myocardial insufficiency. The so-called heat prostration occurring in closed

rooms in the summer are usually not due to heat alone, but depend upon exhausted states of the nervous system, alcoholism, or other causes.

In the caloric diseases the hyperthermia may be very marked; temperatures of 115°-117° F. have been recorded (Lambert). The temperature of the body when the heat-stroke suddenly occurs, is usually about 105° F., and it goes on rising afterward, reaching 109°-111° F. Heat-stroke without elevation of temperature is a misnomer.

Human beings can gradually accustom themselves to high temperatures that would be dangerous to the uninitiated; this is well illustrated by residents in the tropics, and, in temperate zones, by stokers. Clothing is important, as favoring or hindering heat dissipation. Anything which enfeebles the body (alcoholism, obesity, chronic disease of the heart or lungs) favors heat-stroke.

In how far diseases of the nervous system, and of the circulatory system, may depend upon the chronic effects of exposure to high temperatures in overheated rooms, or upon exposure to radiating heat from ovens, or furnaces, among stokers, smelters, cooks, bakers, etc., is not fully known.

Symptoms.—Three stages are distinguishable: (1) the prodromal stage; (2) the heat-stroke proper; and (3) the stage of recovery.

In the PRODROMAL STAGE, there is palpitation, tachypnea, sweating, and rise of temperature to 100.5°-101.5° F. The temperature stays at this level for a time, and then, as a rule, suddenly rises further to around 105° F. at the onset of the stroke.

Before the stroke occurs, various symptoms may appear (headache, vertigo, weakness, nausea or vomiting, congestion of the head, sudden profuse perspiration, or epigastric pain). Some patients complain of paresthesias, dimness of vision, noises in the ears, difficulty in swallowing, or of scintillating scotoma. Sudden cessation of perspiration at this stage is an ominous sign. When such symptoms appear, the heat-stroke can usually be avoided by prompt cessation of work, or by protection from the sun.

The HEAT-STROKE PROPER usually occurs suddenly; the patient becomes mentally disturbed, fainting, showing delirium, or sinking at once into deep coma with loss of reflexes. There is marked tachypnea and tachycardia. Vomiting and diarrhea are common. The urine is scanty or suppressed. Twitching of the muscles, or outspoken convulsions, may appear. The temperature varies now between 105° and 112° F., occasionally r ing 115° or 117° F. If convulsions occur, they may be either g or Jacksonian in type.

Some patients, instead of becoming comatose, exhibit a pecul ium, characterized by convulsions, hallucinations and illusions, ideas, and pressure of activity, symptoms not unlike those ac the toxic deliria of infectious diseases. Such cases o

fatally. In some instances, the fatal cases show, at autopsy, a focal non-purulent encephalitis (Steinhausen), the encephalitic lesions corresponding to monoplegias, hemiplegias or aphasias manifest before death.

Sometimes actual twilight states follow exposure to heat. Passing through the Red Sea on returning from India, in 1899, I saw a delirious stoker rush up from the boiler-room and commit suicide by jumping into the sea. The ship's officers told me that this was not a rare occurrence in those waters.

In the STAGE OF RECOVERY, the patients remain asleep or drowsy for hours or days, periods of semiconsciousness alternating with paroxysmal states of unconsciousness. The patients complain of dreadful fatigue, dizziness, frontal headache, thirst, anorexia, and pains in the muscles. For some time after the attack, pains in different parts of the body, dyspnea, and insomnia may persist. Clonic spasms, cramps in the calves of the legs, neuralgias, and paresthesias are common sequelae. The tachycardia may give way to an outspoken bradycardia, or to arhythmia. Anemia or hemoglobinuria may follow the stroke. Vague neurasthenic symptoms may last a long time, as in the traumatic neuroses.

The principal symptoms in heat-stroke seem to be due to injury to the brain from overheating (either local overheating of the skull, or from effects on the brain from the overheated blood).

The majority of cases recover after a few days or weeks, though, in the severer cases, death may occur, or the recovery be incomplete, owing to actual encephalitic changes.

Edsall's Disease.—A peculiar form of muscular cramp due to exposure to heat, has been especially studied in this country by D. L. Edsall.

Diagnosis.—The history of exposure to heat usually makes the diagnosis easy. Other causes of coma (*alcoholism, hysteria, epilepsy, apoplexy, cerebral malaria, uremia,* etc.) must be considered, in the differential diagnosis.

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B. Diseases Due to Exposure to Cold

The body may suffer from long exposure to cold air, to cold water, or to snow.

If the air be dry, and there be no wind, temperatures of minus 115° F. (− 45° C.) can be borne, without harm, during active exercise. On the other hand, a much higher temperature may be so cold as to be unbearable, if it be accompanied by wind and wet. The danger is greater at high altitudes; mountain climbers often perish in snowstorms. Among predisposing factors may be mentioned, (1) emaciation, (2) anemia, (3) childhood, or senility, (4) non-acclimatization, (5) alcoholism, and (6) insufficient clothing.

As the body temperature falls, the vital functions become paralyzed. Animal experiments and human observations indicate that, when the body temperature falls below 75.2° F. (24° C.), recovery is impossible.

1. Local Effects of Cold

Among the local effects of cold may be mentioned: (1) the anemia and asphyxiation seen in Raynaud's disease (dead fingers); (2) the itching erythema known as chilblains (*perniones*), so common in children and in anemic adults, and affecting especially the acra (fingers, toes, ears, nose); and (3) the local gangrene due to frost-bite, in which the parts have been actually frozen.

2. Death from Freezing

When a patient "freezes to death," the nervous system, the ci system and the respiratory system are the site of the sympt excitability of the nervous system gradually decreases, the ind comes benumbed, his capacity for muscular contraction grow he is overcome by a drowsiness which he cannot resist. The

dim, apathy steals over him, he staggers, and, if left to himself, falls into his last sleep. An initial tachypnea gives way later to slowed respiration, just as the initial tachycardia is followed, later on, by a slow and feeble pulse. If the person be discovered before the respiration and the pulse cease, recovery may still be possible, even though the body be rigid from the cold, provided care be taken to re-warm the body very gradually. Unfortunately, death sometimes occurs quite suddenly, even after recovery of consciousness and return to normal temperature.

3. Cold as a Predisposing Factor

That sudden exposure to cold in people not hardened to it predisposes to certain diseases (pneumonia, influenza, rheumatism) is generally recognized. This predisposing influence seems to be associated with the effects of the cold upon the vasomotor nervous system. Much can be done to harden sensitive persons by systematic vasomotor training through hydrotherapy.

C. Diseases Due to Electrical Injuries

Formerly, injuries due to lightning were the only ones to be considered under this heading. With the great industrial and technical development through electrical energy, a large number of cases of accidental injury from electrical currents have, in late years, been observed.

About 500 people are killed every year by lightning in the United States, and the number of electrical injuries associated with electric lighting, electric railways, dynamos, etc., is constantly growing. In injury from lightning, we have to deal with electric currents of very high tension and of high periodic number.

In order that the body may be injured by an electric current, it must become a part of an electric circuit, either in a bipolar way, through direct or indirect contact with two conductors of different potential, or in a unipolar way, in that the body conducts directly to the earth.

The tension of the current and the strength of the current are important; the higher the **tension**, the greater the danger as a rule, though differences in resistance modify this rule. Thus, one man may, without harm, let a current of a tension of 500 volts pass through him, while another may be killed immediately by a current of only 65 volts (Mohr), owing to differences in resistance at the point of entrance of the current. The **intensity** of the current is much more significant, and this, in turn, is dependent upon the resistance of the body at the site of entrance, and of exit, of the current, and of the conductor.

Electrical injuries occur both with the alternating current and the

direct current. Currents of a tension below 40-60 volts are not harmful. In high-tension currents, the **period-number** is of great importance. Currents with a period-number of 20 to 70 per second are most dangerous, and these include most industrial currents. Currents of up to 1,000 volts, when of high frequency (say 100,000 per second), are devoid of danger and are used for therapeutic purposes (d'Arsonvalisation; Tesla current). If the tension exceed 1,000 volts, such currents may become dangerous, even when of very high frequency, as in lightning. Long contact is much more fatal than brief contact.

Certain occupations are of course peculiarly exposed to electrical injury; thus *death by lightning* is most common among field-workers, *death from currents of industrial electricity*, among electrical engine-fitters and other electro-technical workers. Anyone may, in a town, be accidentally exposed through unipolar contact with a broken live wire.

Very serious accidents sometimes occur in private houses through contact with metals near electric light wires.

Recently I was called to see a young lady, who a few moments before had, on answering a telephone, been thrown violently to the floor, her muscles becoming rigid so that she could not let go of the telephone until her father tore away the connection. The accident was due to contact with an electric lamp wire near by with defectively insulated wiring. Not long ago a young man from Norfolk consulted me with symptoms of traumatic neurosis, following an electrical burn of the hand. He had simply turned on the electric light by a button; he could not let go of this button, and the finger and thumb were burned to the bone!

Lightning is more apt to strike high buildings, or buildings up on hills, than others. Certain trees are more frequently struck than others; thus oaks are more often struck than beeches.

Local Effects.—The effects of electrical injury may be local, or general. The local effects consist of burns of variable degree at the site of entrance, or of exit, of the current. Sometimes the tissues are injured, though the clothing remains intact.

General Symptoms.—Of the general symptoms, those connected with the central nervous system and the sense organs are the more important. In severe electrical injury, the patient cries out and falls unconscious. After a shorter or longer time, if death does not occur immediately, consciousness returns, though the person may behave as though drunk or delirious. Retrograde amnesia is common. Paralyses, or convulsive seizures, follow, as well as various disturbances of sensibility. Vasomotor ances may persist for a long time after the injury.

Respiration is often arrested at first; later, it may be ac Involuntary passage of urine, feces, or sperm may occur.

Sequelae.—As sequelae, an outspoken traumatic neurosis (*q.* develop. In some cases, symptoms pointing to multiple focal

the central nervous system, similar to those of multiple sclerosis, have been observed.

Functional nervous disturbances, following a fright during an electrical storm, are very common among telephone girls in central exchanges.

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D. Diseases Due to Injuries from Röntgen Rays and from Radium

Since röntgenologists have learned to protect themselves and their patients from the injurious effects of the x-ray, burns and injuries due to this physical agent are becoming less common. The gamma rays, produced through the electromagnetic impulse waves of the beta rays of radium, correspond, physically, to x-rays.

Injuries of the body due to such rays depend upon the direct absorption of the rays by the tissues. A certain *intensity of influence* and a certain *length of exposure* are prerequisites to injury. The soft rays are capable of injuring the skin; the hard rays, through their greater penetration, can reach and injure the internal organs. Certain states of the tissues, or of the cells, predispose them to radio-injury; thus young tissues—the lymphadenoid and hematopoietic tissues, and neoplasms—are especially radio-sensitive, while older tissues—muscle cells, nerve cells, connective tissue fibers, etc.—are more radio-resistant. Cells undergoing karyokinesis are particularly sensitive. Histological studies of tissues that have undergone radio-injury reveal marked changes in the cell nuclei (loss of capacity to take on the stain, karyolysis), and, later, degenerative changes in the cytoplasm. Some believe that the rays act primarily by changing the lecithin of the cells, and that the other changes are secondary to the lecithin injury. This view is not out of accord with the fact that certain classes of cells are especially radiosensitive.

1. Röntgen-Injury of the Skin

Burns of all degrees may follow radio-injury. It is customary to divide the effects into four degrees.

Reaction of the First Degree.—At this stage, the signs consist of temporary erythema, followed by loss of hair, desquamation, and slight pigmentation. In some cases, erythema does not appear, though, three weeks after exposure, the loss of hair and the pigmentation occur.

Reaction of the Second Degree.—Outspoken erythema occurs some twelve days after exposure, with itching, or unpleasant, burning sensation, red, or reddish blue, discoloration, and loss of hair. The reaction usually has run its course by the end of the fifth or the sixth week, though permanent changes may follow (atrophy of the skin, telangiectases, scleroderma).

Reaction of the Third Degree.—The skin undergoes a dark, bluish red discoloration. Small papules appear, which change later into vesicles; the latter rupture, and a full-blown moist dermatitis, with formation of scabs and of crusts, develops. The lesions are accompanied by troublesome itching, and by severe pain. On healing, scars, atrophic areas and telangiectases remain.

Reaction of the Fourth Degree.—Occasionally, an x-ray ulcer develops, as a result of deep necrosis of the skin. Such ulcers present a peculiar, glistening, yellow appearance. The borders of the ulcer are irregular. Such ulcers may be extremely painful, and are slow to heal; even when healing in the center, the ulceration may extend by radial outgrowth at the periphery. The patient's general condition may suffer materially (fever, emaciation, psychoses).

2. Chronic Dermatitis Among Röntgenologists

Specialists in x-ray work, who are exposed over and over again through long periods to the x-rays, often develop a chronic dermatitis. The skin becomes rough and dry, and cracks easily. Atrophic patches appear. The finger-nails become irregular and thickened. The skin about the mouth becomes dry and wrinkled, with formation of rhagades. Unfortunately, in many such instances, **carcinoma** develops later on in the altered skin. The tumors may be multiple. Sometimes carcinoma and sarcoma appear in the same patient.

Precautions Against Radio-Injury.—In therapeutic applications of Röntgen rays and of radium, the skin should be carefully protected. The x-rays should be made to pass through an aluminium filter, 1 mm. thick. The dosage should be always accurately measured. (See Methods of Measurement in section on Röntgenology). The intervals between trea

ments must be cautiously arranged. Röntgenologists now wear protective gloves and protective aprons, or have their cabinets so arranged that they themselves are but little exposed to the rays.

3. Röntgen-Injury of the Sex Glands

If the testes of guinea-pigs or of rabbits be sufficiently exposed to the x-rays, the animals become sterile from azoöspermia, though the capacity for the sexual act is otherwise uninjured. When the injury is not too severe, the power of forming spermatozoa may be regained.

In human beings, sterility may also result from exposure, either of the testicles or of the ovaries, to the x-rays. Recently, this fact has been applied therapeutically, in women suffering from prolonged and severe climacteric changes, and also in the treatment of menorrhagia due to myoma of the uterus and to chronic endometritis (Kronig). The results are sometimes remarkable. An especial apparatus is required, with filters permitting of penetration by deep rays, without injury during long exposures. Some gynecologists believe that operations for myoma uteri will no longer be necessary, thanks to this discovery. Great caution should be used in employing x-rays for diagnostic or therapeutic purposes during pregnancy (danger of abortion, or of injury to the child). Drs. Kelly and Burnam tell me that menorrhagia and metrorrhagia will often yield to a few local treatments with radium.

4. Röntgen-Injury of Other Organs

For therapeutic purposes, advantage has been taken of the injurious effects of x-rays upon young, unripe cells in the various forms of leukemia (bone-marrow, spleen, lymph glands). Care is to be exercised in beginning the treatment, lest cell-destruction occur too rapidly and severe intoxication develop (fever, acute gout from nuclein destruction, with setting free of purin bodies; disturbances of nutrition). In a few instances, death has followed such x-ray treatment. Anorexia, albuminuria, diarrhea, pains in the bones, are among the symptoms that sometimes follow injudicious x-ray exposures.

The nervous system seems to be peculiarly resistant to x-ray injury, though patients sometimes complain of various subjective sensations (headache, vertigo, abdominal pain, nausea, diarrhea) after exposure to x-rays. These symptoms rarely occur except in neurotic individuals, and are probably due to suggestive influences. It is asserted that x-ray specialists are especially prone to cardiac, vasomotor, and gastro-intestinal neuroses, and that among them arteriosclerosis occurs earlier than in other individuals.

The thyroid gland appears to be tolerably susceptible to radio-injury. If overexposed to the x-rays, even when normal, symptoms of thyreointoxication may develop. Cautious exposure of the thyroid to x-rays is advocated, by some, in the treatment of Graves's disease. Still better results follow radiation of the thymus in this disorder.

The larger glands of the body (liver, kidney, pancreas) seem to be highly radio-resistant.

In animals, growth may be arrested by exposure to radium or to x-rays. Human beings seem to be less susceptible, though until we know more about the subject, it would be wise to avoid any unnecessary exposure of young children to either x-rays or radium.

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E. Diseases Due to Alterations in Atmospheric Pressure

Knowledge regarding the pathological states resulting from changes in atmospheric pressure has grown largely in recent years. The bodily functions are accustomed to an atmospheric pressure that varies but little, either above or below 760 millimeters of mercury. A sudden increase of atmospheric pressure causes unpleasant sensations in the ears, due to increase in the difference between the pressure in the middle ear and in the external auditory canal. Everyone who has gone through the tunnel leading under the river into New York, by fast train, is familiar with this feeling.

Sometimes when the difference in pressure is great, the ear drum ruptures; this has occurred in persons near explosions. In the terrible World War (1914), going on as I write, it is reported that many soldiers are found dead without any signs of trauma on their bodies, death being due, presumably, to air-pressure changes near bursting shells.

Diminution of atmospheric pressure varies in its effect according to whether it occurs suddenly, or slowly. On sudden diminution, changes occur in the ear and in the paranasal sinuses. A good deal depends upon whether, before the diminution in the pressure, the body has been exposed to a higher pressure than normal; thus, when the animal body is exposed to a pressure of two atmospheres or more, large amounts of gas become

dissolved in the body fluids. If, then, the pressure be suddenly lowered, a large part of this gas goes out of solution. The oxygen and the carbon dioxid may remain chemically bound, but the nitrogen appears in the form of bubbles in the blood and lymph, and may mechanically injure the tissues (caisson disease, diver's disease). Similar changes occur when the body, exposed to ordinary atmospheric pressure, is suddenly placed in an environment in which the pressure is less than half an atmosphere (balloon ascension, aviation). In such instances, symptoms of oxygen-hunger appear, owing to insufficient arterialization of the blood due to the lessened pressure of oxygen. Similar oxygen-hunger may arise when the atmospheric pressure is slowly reduced, as in mountain climbing and in residence at high altitudes (mountain sickness), though in many instances compensatory processes rapidly set in (polyglobulia), which make the conditions tolerable.

1. Caisson Disease

When the pressure has been very high in a caisson and is then suddenly lowered, the workmen may become ill. Two forms, one milder, the other more severe, are distinguished.

In the **milder form** of caisson disease, the workmen, after a few minutes or a few hours, complain of abdominal pain and of pains in the joints of the extremities ("bends"). The arthralgia is most pronounced in the knees, though the elbows and hips are also often affected. The Valleix points are tender. Epistaxis is common. The patients may be nauseated.

In the **severer form**, the pains in the extremities become so severe that the limbs are immobile; there is retention of urine and feces, and all the signs of spastic paraplegia may develop; this may be partial and temporary, or more complete. In the latter case, death may follow from bedsores, or from infection of the urinary passages. Instead of spinal symptoms, cerebral or cerebellar phenomena may predominate (vertigo, cerebellar gait, Ménière attacks, delirium, and other psychic disturbances, partial blindness, aphasia, diplopia, deafness, partial paralysis). In other instances, the symptoms are those of a traumatic neurosis (*q. v.*).

Caisson workers should be protected by law from too speedy decompression. For each tenth of an atmosphere of decompression, at least one minute of time should be allowed. Where the pressure is very high, the decompression should take place even more slowly, or the method of gradual decompression suggested by Boykott, Damant and Haldane should be used.

Now that the cause of the disease is known, many patients in whom symptoms have appeared can be saved by placing them, immediately, under high pressure again, and then proceeding, extremely cautiously, with the decompression.

2. Diver's Disease

The conditions are similar to those of caisson disease, except that the pressure is lower, and the time of exposure to high pressure shorter. Though there is less danger here, accidents are not uncommon because fewer precautions are taken than among caisson workers. Professional divers in the navy, in pearl fisheries, and in sponge fisheries, are subject to this disorder. Much can be done to prevent the disease by the use of diving apparatus that prevents too rapid decompression.

3. Air-Pressure Diseases Among Balloonists and Aviators

When balloonists rise above an altitude of 4,000 to 5,000 meters, symptoms of air-hunger appear; at an altitude of 8,000 meters, death may occur, the individual going gradually to sleep (cerebral paralysis). Life can be maintained at altitudes of 10,000 to 12,000 meters by breathing pure oxygen, but even with this preventive attacks of syncope occur.

Even at relatively low altitudes, tachycardia and tachypnea appear; the circulation and respiration are so impeded by the shoving up of the diaphragm, due to expansion of gas in the stomach and intestines.

Aviators suffer at a lower level than balloonists, owing to the concentrated attention required of the pilot interfering with deep respiration, and to the increased amount of oxygen required owing to his muscular exertion (von Schrötter). The speed of ascent is an important factor, as it gives but little time for readjustment to the lessened oxygen-pressure. On landing after a flight, aviators suffer from vasomotor disturbances, with marked rise of blood pressure; they complain of palpitation, congestion of the head, dizziness, and drowsiness. The aviator, Chavez, after flying over the Alps, died of myocardial insufficiency with severe delirium, two days later. It is true that, at the end of his flight, he fell and broke both legs, but his death is attributed to vasomotor disturbances, due to the diminution of atmospheric pressure during his flight, rather than to the fractures.

4. Mountain Disease (Acosta's Disease)

Travelers at very high altitudes (Andes, Himalayas) may suffer from excessive fatigue and drowsiness. There is retching, and vertigo. In addition to palpitation and shortness of breath,

be hemorrhages from the mucous membranes and fever. In the severe cases, the patients pass into coma and die. The disease was first described by a Jesuit Father, Acosta, who observed it during his travels at a high altitude in Peru (1590).

Most patients recover, even at the high altitude, if they remain quiet. The symptoms are usually over in a week or two, though with many patients it may be months before they feel well again. The disease most often attacks patients with weak hearts, and those who are under-nourished or over-fatigued.

Various theories have been advanced to account for the disease. The true explanation seems to lie in the diminution of the oxygen-tension in the pulmonary alveoli, and the resulting incomplete saturation of the hemoglobin with this gas (Paul Bert). Some individuals are more susceptible than others, probably owing to variations in the regulatory mechanisms controlling the oxygen supply to the various organs.

The true mountain disease is, of course, not to be confused with myocardial insufficiency, or with cerebral apoplexy, occurring at high altitudes.

Physicians should always be careful, in giving permission to patients to visit high altitudes, to instruct them how to travel. In increasing the altitude as much as 1,000 meters, a day or two should be spent at some half-way place, on the way up, if there be any doubt as to the strength of the heart. If any symptoms, either of circulatory disease or of true mountain disease, appear, they will usually pass off if the patient remain at absolute rest in bed for a few days at the level at which he finds himself inconvenienced, or he may be quickly and cautiously transported to a lower level. It is surprising to what altitudes human beings can accustom themselves, if they go about it cautiously.

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F. Diseases Due to Unaccustomed Movements, or to Alterations of the Direction of the Movements of the Body (Sea-Sickness, Car-Sickness, Kinetoses)

When the human body is subjected to movements, or to alterations of the direction of movements, to which it is unaccustomed, it often reacts with a peculiar set of symptoms of a functional nervous nature (mental, gastric, circulatory). Among the conditions that give rise to these unpleasant sensations may be mentioned (1) the movements of boats, or of ships, at sea (sea-sickness), and (2) the movement of trains along sharp curves (car-sickness). Slight sensations, allied to the more severe disturbances, are often experienced in swings, in elevators, on merry-go-rounds, or during earthquakes. Undoubtedly, psychic influences may play a part in the production of the symptoms, but in the majority of cases true somatic disturbances are concerned also.

Sea-Sickness

Occurrence.—The movements of the ship most likely to cause symptoms are (1) "pitching" and (2) "cork-screw-like motion," while "rolling" is less likely to cause them. During pitching, it is the moment just after the ship has risen and begins to sink again that is associated with that unpleasant feeling in the epigastrium which immediately nauseates many people, and is followed by vomiting and retching. The larger the ship, as a rule, the more steady it is; the nearer the center of the ship, the less the motion. Individual susceptibility varies greatly, though nearly everyone will be attacked when the movements are extreme. Women are more susceptible than men. Infants and very young children rarely suffer. Disturbances of digestion and alcoholic excess predispose.

Symptoms.—The mental state is characteristic (ill-humor, apathy, depression, disinclination for conversation). Among the somatic symptoms, headache, dizziness and nausea appear early. The patient turns pale, and breaks out into a cold sweat; the eyes become fixed; and, finally, vomiting occurs, sometimes giving relief to the symptoms. Some patients are not relieved by vomiting, but are nauseated continuously, and, with every movement of the ship, suffer from violent retching; this, when the stomach is empty, is often harder to bear than vomiting. Constipation and leucorrhea are common. The skin is cold and clammy, despite the sweating.

People rarely die of sea-sickness, though many long to die of it. As the sea becomes smoother, the symptoms let up; even when it continues rough, persons usually grow accustomed to the movement; they "get their sea-legs on."

Deaf-mutes, made so from labyrinthine disease, are said to be insusceptible to sea-sickness. The essence of the disease appears to consist in disturbances of equilibrium, and in disorientation in space, due (1) to rapid changes in optic impressions, (2) to abnormal stimulations of the vestibular apparatus, and (3) to irritation of the abdominal sympathetic, following the movements of the ship.

Ocean travel is less to be feared than formerly by those subject to sea-sickness, owing to the many mechanical devices which now limit motion, and to the increased size and comfort of the trans-oceanic liners. Travelers have also learned the importance (1) of staying on deck, in the fresh air, (2) of the assumption of the recumbent position, on deck, in the middle of the ship, and (3) of the wearing of an abdominal band. Courage, a certain tension of the will, the avoidance of all excess in food and drink, and guarding against constipation, go far toward preventing the disorder.

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Part V.

Diagnosis of Diseases of the Respiratory Apparatus

Section I

METHODS OF EXAMINATION

The methods of examination of the organs belonging to the respiratory system will first be taken up, after which the diagnosis of the special diseases of this system will follow.

Under the respiratory apparatus we include, (1) the *nasal cavity* (*cavum nasi*), (2) the *larynx*, (3) the *trachea* and *bronchi*, (4) the *lung* (*pulmo*), and (5) the *pleural cavity* (*cavum pleurae*), that on the right being separated from that on the left by the *mediastinal septum* (*septum mediastinale*).

The **nasal cavity** opens in front through the *nares*, or anterior apertures, and behind it communicates with the pharynx through the *choanae*, or posterior apertures. The *septum nasi*, or nasal septum, divides the cavity into two halves. Part of this septum is bony, part cartilaginous, and part membranous. The wall of the nasal cavity is lined by mucous membrane (*membrana mucosa nasi*). On the lateral wall of the nasal cavity are the three turbinated bones, or *conchae*. These include the superior, the middle, and the inferior nasal conchae. Below each concha, and lateral from it, is a meatus (*meatus nasi superior, medius,* and *inferior*).

Connected with the nasal cavity are certain accessory cavities known as the *paranasal sinuses* (*sinus paranasales*). Their openings into the nasal cavity are described further on. These sinuses include the maxillary sinus, or antrum of Highmore (*sinus maxillaris* [*Highmori*]), the sphenoidal sinus (*sinus sphenoidalis*), and the frontal sinus (*sinus frontalis*) on each side. In addition, the ethmoid cells (*cellulae ethmoidales*), and the ethmoidal bulla (*bulla ethmoidalis*) belong here.

The portion of the nasal cavity connected with the sense of smell is a small area on the upper part of the superior concha and on the adjacent septum (*regio olfactoria*). The rest of the mucous membrane is thinner (*regio respiratoria*).

The **larynx** possesses a *cartilaginous framework*, including the thyroid cartilage, the cricoid cartilage, the arytenoid cartilage, the cartilage of the epiglottis, and the minute corniculate cartilages of Santorini and the cuneiform cartilages of Wrisberg. These cartilages are held together by means of ligaments and joints. The *intrinsic muscles* of the larynx include the M. cricothyroideus, the M. crico-arytenoideus posterior, the M. crico-arytenoideus lateralis, the M. thyro-arytenoideus,

the M. epiglotticus, the M. arytenoideus obliquus, the M. vocalis, the M. ventricularis, and the M. arytenoideus transversus.

The *cavity of the larynx* is covered by mucous membrane (*tunica mucosa laryngis*). The ventricle of the larynx is a deep groove, bounded by two folds:—(1) the *plica vocalis,* or true vocal cord, and (2) the *plica ventricularis,* or false vocal cord. Between the two *plicae vocales* lies the slit of the glottis (*rima glottidis*), consisting of a longer anterior portion (*pars intermembranacea*), and a shorter posterior portion (*pars intercartilaginea*).

The **trachea** begins opposite the seventh cervical vertebra and undergoes bifurcation opposite the fourth or fifth thoracic vertebral body into the two *bronchi.* In the trachea there are 16-20 horseshoelike strips of cartilage (*cartilagines tracheales*).

There are two **bronchi,** one on the right side (*bronchus dexter*), and one on the left side (*bronchus sinister*). The finer subdivisions of the bronchi are known as bronchioles (*bronchioli*). Each bronchiole opens through an *alveolar duct* and *atria* into the air sacs, and the whole surface of each of these sacs is studded with minute cavities known as pulmonary alveoli (*alveoli pulmonis*). The lobule of the lung (*lobulus pulmonis*) is made up of one alveolar duct with all the sacs and alveoli given off from it.

Each **lung** possesses a blunt tip (*apex pulmonis*), and a broad base (*basis pulmonis*). Each lung presents three surfaces, one in contact with the diaphragm below (*facies diaphragmatica*), one in contact with the ribs (*facies costalis*), and one directed toward the pericardium and the mediastinum (*facies mediastinalis*). The inferior margin of the lung (*margo inferior*) lies at the junction of the costal surface with the diaphragmatic surface, while the anterior margin of the lung (*margo anterior*) lies at the junction of the costal surface with the mediastinal surface. The bronchi, blood vessels and nerves enter into relation with the lungs at a fossa on the mediastinal surface known as the *hilus pulmonis.* The structures here, including the pulmonary lymph glands, are known as the root of the lung (*radix pulmonis*).

The upper lobe (*lobus superior*) of each lung is separated from the lower lobe (*lobus inferior*) by a deep fissure (*incisura interlobaris*). On the right side a second fissure goes off from the main incisure in a horizontal direction at the level of the fourth intercostal space; the portion of lung between this and the main incisure is known as the middle lobe (*lobus medius*).

In the anterior margin of the left lung there is a deep notch (*incisura cardiaca*) opposite the heart. The narrow portion of the upper lobe that projects forward below this notch is called the *lingula pulmonis.*

Each **pleural cavity** (*cavum pleurae*) is a slitlike space lined by a smooth serous membrane (*pleura*). This pleura is divisible into a part that covers the lung (*pleura pulmonis*) and a part that lines the walls of the thoracic cavity (*pleura parietalis*). The latter is divisible into (1) the costal pleura (*pleura costalis*), which covers the inner surface of the ribs, vertebrae, sternum, thoracic muscles, etc.; (2) the diaphragmatic pleura (*pleura diaphragmatica*), which covers the upper surface of the diaphragm, and (3) the mediastinal pleura (*pleura mediastinalis*), which covers the mediastinal septum; a part of the latter, fused with the pericardium, is often called the pericardiac pleura (*pleura pericardiaca*), whereas the rest of it is known as the mediastinal layer (*lamina mediastinalis*). The pleural cavity ends, above, in a blind saclike prolongation known as the *cupula pleurae.* At the lower part of the pleural cavity the diaphragmatic pleura lies in contact with the costal pleura, thus bounding the *sinus phrenicocostalis;* on inspiration, the lung passes into this *sinus pleurae,* but never as far as the line of reflection.

The **mediastinal septum** (*septum mediastinale*) is divisible into a smaller, ante-

rior portion (*spatium mediastinale anterius*), and a larger, posterior portion (*spatium mediastinale posterius*). In the former lie the internal mammary arteries and veins, the phrenic nerves, the thymus, and certain lymph glands; while in the latter are situated the thoracic aorta, the intercostal arteries, the azygos and hemiazygos veins, the thoracic duct, the pneumogastric and the splanchnic nerves, the esophagus, and certain lymph glands. The functions of this mediastinal septum and its weak spots are described further on.

A. Examination of the Nose and the Paranasal Sinuses

The interior of the nose may be examined from the front (*anterior rhinoscopy*), or from behind through the choanae (*posterior rhinoscopy*).

1. Anterior Rhinoscopy

The nasal orifice is held as wide open as possible by means of a bivalve nasal speculum, care being taken to avoid causing pain. It is essential to have a satisfactory illumination of the parts under examination. The examiner wears the ordinary reflecting head mirror, looking through the hole in its middle. A good lamp, gas-flame, or electric light serves as a source of light behind and at one side of the patient, on a level with his head; the light-rays and the rays of the image should go nearly parallel to one another. In the physician's office, a Coakley-McKenzie electric light stand with large McKenzie condensor is convenient. Still better is the use of an electric light (dry-cell battery) on a metal head-band; then no reflecting mirror is required. The patient and the examiner sit opposite each other on chairs, and so close to each other that the legs of the patient are between the knees of the observer. The mirror, or the head-light, is arranged so as to give the best illumination possible. The patient's head is held and directed by the examiner's one hand while he manipulates the *nasal speculum* with the other. The blades of the speculum are inserted, closed, into one nostril, and then opened gently; pain should be caused. A regular routine should be followed. One exa

Fig. 132.—Electric Light on Metal Head-bands. (After H. O. Reik.)

(1) On the medial side, the surface of the *nasal septum*, noticing curves, spurs, crests, or deflections, as well as ulcerations or perforations, if present.

Fig. 133.—Bivalve Nasal Speculum. (After H. O. Reik.)

(2) On the lateral side, separated from the septum by a broader, or narrower, interspace: (a) the *inferior concha*, or *turbinated bone*, the anterior end of which is easily visible; (b) the anterior extremity of the *middle concha*, or *turbinated bone*, better seen when the patient's head is inclined slightly backward; (c) the *middle meatus*, or nasal passage, situated between these two conchae, in which lie the important openings (1) into the *sinus maxillaris* (antrum of Highmore) and (2) into the *sinus frontalis;* (d) the *inferior meatus*, below the inferior conchae, and (e) the narrow slit (*rima olfactoria*) lying between the middle concha and the septum.

In case the nostril is occluded, or is very narrow from swollen conchae, the examination is facilitated if the swelling is reduced by the application of a wad of cotton soaked in cocain solution (4-10 per cent) to which a few drops of 1/10 of 1-per-cent solution of adrenalin chlorid have been added. As adrenalin is very irritating to the nasal mucous membrane, it is often better to avoid its use, and to depend upon cocain or menthol as shrinking agents.

One should look carefully for an *abnormal outflow of secretion* below the middle concha (*hiatus semilunaris*); by bending the patient's head forward and toward the opposite side, the outflow will be favored in some instances, interfered with in others, or one may compress the bulb of a Pollitzer air bag, introduce the nozzle into the nostril, and by suction try to make pus or abnormal secretion exude from the openings. When secretion is present on first inspection, it is well to wipe it off and then see if more appears.

When the *conchae are enlarged*, it is necessary to determine whether the swelling is due simply to *hyperemia*, or to so-called *"hypertrophy"*; hyperemic swellings disappear under cocain and adrenalin, and are soft when palpated with the nasal sound. One notes, further, the presence or absence of *polypi* and of *tumors*, the character of the *mucous membrane*, and the *size* of the nasal cavity. *Foreign bodies*, if present, will be visible.

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[For other references, see Special Diagnosis of Diseases of the Nose.]

2. Posterior Rhinoscopy and Pharyngoscopy

Using the same head mirror, or an electric head-light, one places a small, plain, long-handled mirror, previously warmed (tested against overheating on the back of the hand), behind the soft palate, so that its surface looks forward and upward. The patient is told to breathe through his nose, as this relaxes the soft palate; meanwhile, the tongue is held down by a spatula or a depressor. Care should be taken not to touch either the soft palate or the posterior pharyngeal wall with the mirror, otherwise gagging occurs. The mirror should be almost at right angles to the handle, the latter being held towards the angle of the mouth, to get it out of the line of vision. If desired, a mirror, the inclination of which may be altered by pressure on the handle, may be used. If necessary, the soft palate and the wall of the pharynx may be cocainized, or the uvula and soft palate may be drawn forward with a hooked spatula. Sometimes a better view is obtained if the patient be asked to say "hah," in a nasal tone. Here again, the examination of the parts should be systematic, while the rhinoscopic mirror is tilted into different positions, as follows:

(1) The *choanae,* or posterior orifices of the nasal cavities, separated from one another by the light-colored, perpendicular, posterior border of the septum (vomer).

(2) The posterior ends of the *inferior conchae* or *turbinated bones,* projecting from the sides into the choanae.

(3) Above them, less distinctly visible, the *middle conchae,* and sometimes the *superior conchae.*

(4) Turn the mirror sidewise so as to examine the lateral walls of the nasopharynx and look for a reddish-yellow bulging, presenting a pale, funnel-shaped indentation at its middle; this is the *orifice of the eustachian tube* (*tuba auditiva*). Above and lateral from the tube-projection is a dark depression, known as *Rosenmüller's fossa.* The structures should be examined first on the right side, and then on the left.

(5) If the surface of the mirror be now turned still further upward, the *roof of the pharynx* will become visible, including the origin of the *pharyngeal tonsil.* Hypertrophy of this (*adenoid vegetations*) will be

visible as ridges or as stalactite growths. In children, they often interfere seriously with nasal breathing.

(6) Note especially the presence or absence of *pathological secretion,* of *ulcers,* of *hypertrophied conchae,* and of *tumors.* Sometimes, a tumor originating in the hypophysis cerebri (sella turcica) projects into the nasopharynx. The nasopharynx can be still more easily inspected with the aid of *Hay's electric pharyngoscope.* (See Examination of the Larynx).

3. Sinusoscopy

In rare instances, it may be desirable to examine the maxillary sinus (antrum of Highmore) by means of a small instrument, a *sinusoscope,* built on the principle of the cystoscope; an instrument of 4 mm. in size can be introduced into the antrum, through a hole bored through the alveolus of a tooth. The same instrument can be used for examination of special parts of the nasal cavity and of the nasopharyngeal space.

4. Palpation of the Nose and Nasopharynx

Through the nasal speculum, the *consistence* of abnormal structures can be felt by means of a *sound,* the end of which is protected by a little cotton soaked in borax solution; one can thus easily distinguish between the soft nature of hyperemic conchae and the tough hypertrophy and hyperplastic conditions of these structures. There is often *tenderness* on pressure in the fossa canina when the *antrum* is diseased, and at the root of the nose and the adjoining portions of the frontal bone when the frontal sinus is affected. *Tenderness over the frontal sinus* in sinusitis can most often be elicited by pressure on the floor of the sinus; we ask the patient to look down, so as to get the upper lid out of the way; the finger is then pressed upward between the eyeball and the orbital roof as deeply as possible, avoiding pressure on the N. supra-orbitalis.

Palpation of the nasopharynx is especially valuable in young children, where posterior rhinoscopy may be difficult or impossible. Making sure that the nail on the fore-finger of the right hand is cut short, one disinfects the finger carefully, or covers it with a sterile finger-cot, and, placing the child on a stool, holds its head firmly with the left hand; the examining finger is then introduced between the soft palate and the posterior wall of the pharynx and passed upward into the nasopharynx. It is easy to feel the *roof* of the pharynx, and the *tubal projections;* and one can determine at once whether or not the *pharyngeal tonsil* is hypertrophied, or whether all is smooth. One can easily avoid being bitten, by placing, with the examining hand, the lower lip of the patient over the lower front teeth.

5. Transillumination of the Paranasal Sinuses

This is especially valuable for the examination (1) of the sinus laris, or antrum of Highmore, and (2) of the frontal sinuses. The m requires a small *electric light,* on a suitable *holder,* and the exami must be made in a *dark room*, or under a *canopy* that shuts out da

To transilluminate the maxillary sinuses, the electric light is inside the patient's mouth and the patient is instructed to close h on the holder. If one antrum contain pus, or if its mucous mem be greatly thickened, more light will be absorbed by the disease than by the healthy side, and the former will look much darker the other.

A similar method may be employed for examining the frontal si An electric lamp, provided with a lens and screened by a rubber c pressed close against the skin at the medial upper margin of the orbi one frontal sinus be diseased, the illumination will be less widespre that side than on the healthy side.

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6. Röntgenography of the Paranasal Sinuses

By observation of a careful technic, it is often possible to recogni existence of disease of one or more of the paranasal sinuses (max frontal, ethmoidal, sphenoidal) by the appearance of dark shado corresponding situations, in the x-ray plate. The etiology of c cephalalgias and trigeminal neuralgias, and of many cases of met infection (arthritis, nephritis) is, occasionally, made clear by th covery of previously unsuspected sinus disease.

Röntgenography of the Frontal Sinuses.—The patient lies on h with his arms and hands along the edge of the table. In order to the strong shadows thrown by the temporal bone, a photograph is ta throwing the pyramid of Röntgen rays in a direction from abo occipital protuberance behind, toward the orbit in front. The s middle plane of the head should be perpendicular to the photog

plate; this is difficult, but very important, in order to avoid deceptive shadows. The forehead and nose should rest upon the plate. Or, the photograph may be taken in the sitting posture, if the head be firmly held in position either by a clamp, or by sandbags in a box standing on a table in front of the sitting patient; in the sitting position, the head contains less blood than in the recumbent posture, and a clearer negative is obtained.

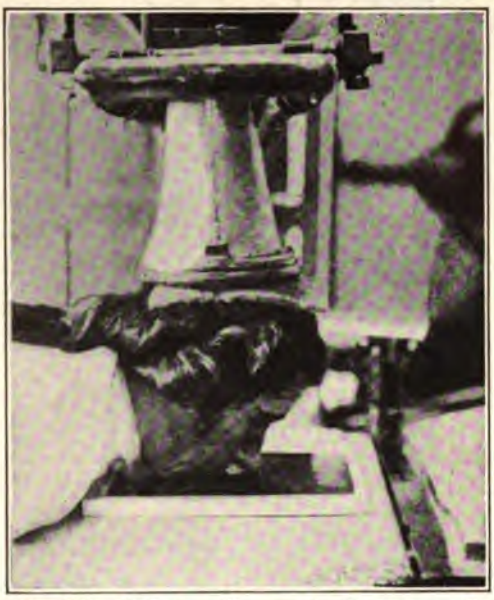


Fig. 134.—Patient in Position for Röntgenography of the Paranasal Sinuses. (After C. A. Waters and C. W. Waldron, Am. J. Röntgenol.)

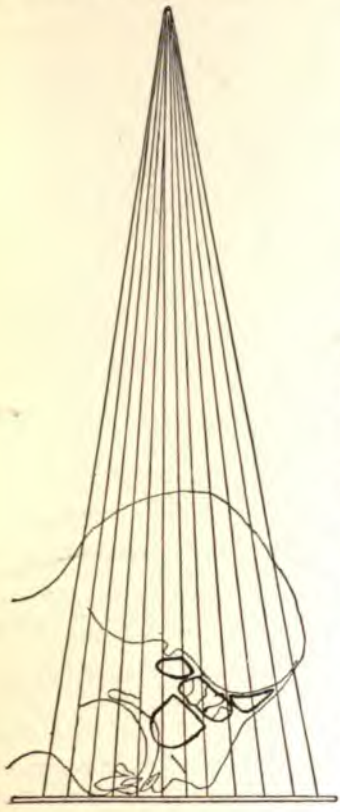
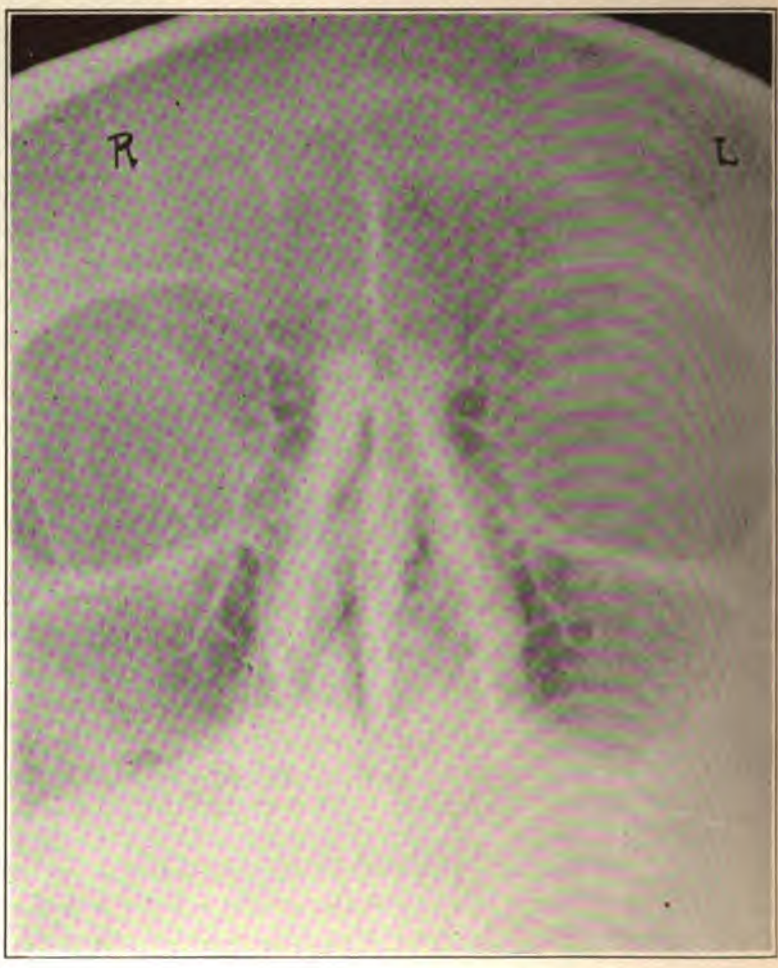


Fig. 135.—Diagram Illustrating Projection of Rays upon the Photographic Plate in the Anteroposition Plane During Röntgenography of the Paranasal Sinuses. (After C. A. Waters and C. W. Waldron, Am. J. Röntgenol.)

Röntgenography of the Maxillary Sinuses.—The negative may be made either in the recumbent or in the sitting posture, as above described. But the pyramid of rays is now directed from behind so that the center of the bundle of rays passes through the middle line, where it cuts a line passing through the middle of the posterior margins of the ascending rami of the mandible; passing forward, the center of the bundle of rays will then emerge in front at the middle of the dorsum nasi. Since disease of the antra sometimes depends on lesions at the roots of the teeth, special röntgenograms of these may also be desirable. (See Digestive System.)

Röntgenography of the Ethmoidal and Sphenoidal Sinuses.—By especially carefully arranged postures, these sinuses can also be photographed. The sphenoidal sinus shows well in lateral views of the



g. 136.—Röntgenogram of Normal Paranasal Sinuses in the Adult. The Frontal Sinuses are Large and Show Orbital Extensions; the Anterior and Posterior Ethmoidal Cells are Well Defined; the Maxillary Sinuses are Well Developed; there is an Air Cell in the Crista galli. See Fig. 137. (After C. A. Walters and C. W. Waldron, Am. J. Röntgenol.)

ull, such as are made to reveal the sella turcica (*q. v.*). Here the rays ıter in the region of the external auditory canal.

Waters and Waldron (1915) have published an important paper on röntgenogphy of the paranasal sinuses, describing a new technic which affords greater effiency in diagnosis. The occipitofrontal position, first used by Caldwell in America, d by Killian in Germany, has been slightly modified by them so that a single ntgenogram reveals clearly the frontal and maxillary sinuses and the anterior d posterior ethmoid cells on the same plate without obscuring the outlines of the tra by shadows of the petrous portions of the temporal bones. The patient lies a horizontal table with his face downward and the chin resting on a cassette, ıich holds the plate and an intensifying screen. Upon the occiput, a compression

diaphragm 18 cm. deep is screwed down tightly, a felt pad 2 cm. in thickness being interposed. Three rules are emphasized, (1) the chin must rest upon the plate, (2) the long axis of the tube must be parallel to the plate, and (3) the nose of the patient should be from 1 to 1.5 cm. from the plate, under no condition touching it. Two distinct types of face (the concave and the convex) are distinguished, requiring a variation of an angle of about 2° in the vertical axis of the skull. With a concave face, the course of the base of the skull is high, necessitating an increase of ½ cm. in the distance of the nose from the plate. The authors recommend keeping the nose of the concave face 1.5 cm. distant from the plate, while with the convex face the nose is placed only 1 cm. distant, with the long axis of the tube still parallel to the plate. A moderate milliampèrage is employed as well as a soft tube with intensifying screen, since these conditions yield the greatest amount of detail. They have employed the method in 1,000 cases and are firmly convinced of its superiority from the diagnostic standpoint.

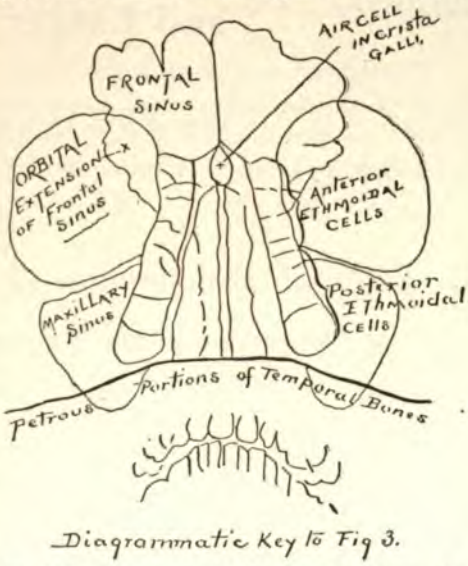


Fig. 137.—Diagrammatic Key to Preceding Figure, Illustrating a Röntgenogram of Normal Paranasal Sinuses in Adult. (After C. A. Waters and C. W. Waldron, Am. J. Röntgenol.)

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7. Sounding the Maxillary Sinus

The passage of sounds into openings of the several paranasal sinuses, and the exploratory puncture of the maxillary sinus, or antrum, from the inferior meatus nasi, are methods sometimes employed for diagnosis; for a description of these special text-books and monographs may be consulted.

B. Examination of the Larynx, Trachea and Larger Bronchi

The larynx and trachea are visible, especially in thin people, in the front of the neck (*external examination*). With the aid of specially devised instruments, it is possible also to inspect the interior of the larynx (*laryngoscopy*) and the trachea and larger bronchi (*bronchoscopy*).

1. External Examination of the Larynx and Trachea

(*a*) *Inspection of the Larynx and Trachea Externally*

The larynx lies normally between the upper margin of the third and the lower margin of the sixth cervical vertebra; during respiration, phonation and deglutition, it rises to higher, and descends to lower, levels. On external examination, one pays attention to the *size, form,* and *position* of the larynx (and trachea), especially to lateral displacements, and to rotations of the larynx as a whole. Marked swelling may be visible in perichondrial inflammations.

The *respiratory movements of the larynx* are diminished in stenosis of the trachea or of the large bronchi, the head tending to be bent forward, while in stenosis in the larynx itself, the head is inclined backward and the respiratory movements of the larynx are markedly increased. In inflammatory and edematous conditions of the larynx (diphtheria, edema of the glottis, tumors, paralysis of the openers of the glottis, spasm of the closers of the glottis), respiration is difficult, the breathing being slower than normal, inspiration, especially, being long-drawn-out and accompanied by a rough noise (*stridor*).

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Killian* (*G.*).** *Schwebelaryngoskopie. Arch. f. Laryngol. u. Rhinol., Berlin,* ***1912, *xxvii, 277–317. 1 pl.*

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(*b*) *Palpation of the Larynx and Trachea*

On palpation, the consistence of swellings of the thyroid an cartilages may be examined, and tenderness on pressure sought fo cially important, here, is the examination for the presence of a **tracheal tug** (Oliver-Cardarelli sign). In aortic aneuri shocks are transmitted to the trachea; sometimes these are v are most easily recognized by placing the thumb an

beneath the cricoid cartilage while the patient inclines his head somewhat backward, in order to make the structures in front of the neck a little tense. If a tracheal tug is present, the fingers will detect a cardiosystolic tug upon the larynx.

(c) *Percussion of the Larynx*

On percussion, the larynx yields a tympanitic sound, the pitch of which is higher when the mouth is open, lower when the mouth is closed.

(d) *Auscultation of the Larynx and Trachea*

On auscultation with the stethoscope over the larynx and the trachea, very loud tubular breathing is normally audible (laryngeal and tracheal breathing).

With the naked ear, one should pay attention to the sounds produced by the larynx on phonation, as they are of some value in diagnosis. Difficulty in speech, due to disturbance of the respiratory passages, is known as *dysphonia;* inability to speak above a whisper as *aphonia,* or loss of voice.

Dysphonia may be due to inability to expel a forcible current of air through the larynx (feeble voice); this is often seen in diseases of the air passages, as well as in some paralyses of the vocal cords. When high and low tones cannot be produced, the voice becomes *monotonous*, and when abnormal accessory sounds accompany the voice it becomes *hoarse.*

Aphonia, or loss of voice, is very common in hysteria, but may appear temporarily in inflammatory conditions of the larynx. In certain laryngeal diseases, either a falsetto (unnaturally high and piping), or a deep bass voice, may appear. The peculiar phenomenon known as double voice **(diplophonia)** is met with in polyp of the larynx; during phonation, the polypus becomes engaged between the free margins of the vocal cords, and gives rise to different vibrations in the two portions of the cords. A peculiar *nasal twang* in the voice, especially in pronouncing *m*, *n* and *ng* (ask the patient to say "Good-morning"), is due to obstruction in the nose or nasopharynx (*hypertrophies, tumors, adenoids*). An opposite condition is met with in paralysis of the velum palatinum; the nasal cavities cannot be closed off from the mouth cavity on speaking, and one then hears the so-called "open nasal voice," the nasal twang being prominent and causing difficulty, especially in the pronunciation of the explosive letters, *b, p, k* and *t.*

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2. Internal Examination of the Larynx (Laryngoscopy)

The most important method of examining the larynx is by inspection of the interior; this may be done directly (*direct laryngoscopy* or *autoscopy*), or indirectly through a mirror (*ordinary* or *indirect laryngoscopy*). The latter method is by far the more important.

(*a*) *Direct Laryngoscopy*

This may be carried out, either (1) by the autoscopy of Kirstein, or, better, (2) by the use of Hay's electrical pharyngoscope.

i. Autoscopy of Kirstein

The patient, seated in a chair, bends his head well backward, so as to make as direct a line as possible from the mouth-opening to the larynx. The examiner presses the base of the tongue forward and backward with a strong spatula, until the posterior half of the larynx becomes visible (electric illumination with Kirstein's lamp). The method is uncomfortable for the patient, but often affords a very satisfactory view, especially of the back of the larynx. In children, it is sometimes the only method of getting a view of the larynx. The procedure is occasionally resorted to when operations are performed upon the larynx under anesthesia.

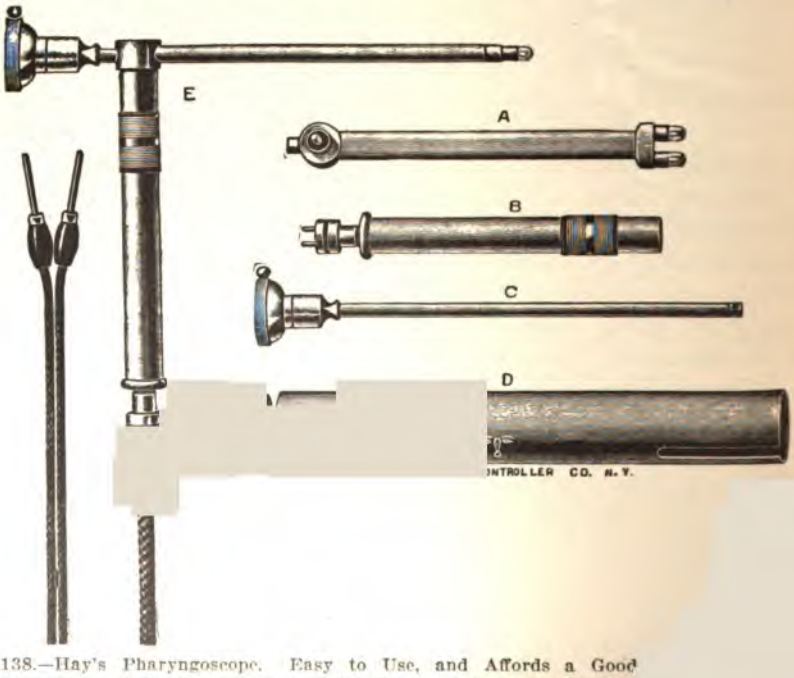

Fig. 138.—Hay's Pharyngoscope. Easy to Use, and Affords a Good Illumination, of the Nasopharynx, Tubal Orifices and the Larynx. (

ii. Direct Laryngoscopy with Hay's Pharyngoscope

Direct inspection of the interior of the larynx has been made comparatively easy by the invention of this ingenious instrument. The apparatus (Fig. 138) is a modified form of telescope. The tube of the instrument depresses the tongue. At the inner end of the tube is a small electric lamp and a very small reflecting mirror, which can be rotated by moving a knob on the handle. At the outer end of the tube is the eye-piece through which the examiner peers. Bright illumination is obtained by attaching the instrument to a wall-socket controller.

Instead of Hay's pharyngoscope, the instrument of Holmes or that of Schmuckert may be used if preferred.

Fig. 139.—Schmuckert's Electric Pharyngoscope. (By courtesy of the Kny-Scheerer Co.)

Technic. — The tube is passed over the tongue into the pharynx, and the patient closes his mouth. By turning the mirror in different directions, one can, at his leisure, view (1) the interior of the larynx, (2) the vault of the pharynx, and (3) the lateral regions of the pharynx, including the orifices of the eustachian tubes. After a little practice, excellent views are obtainable. Along with a small portable dry battery, this instrument can be carried in the consultation bag, and used in house visits where no other electric current is available.

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(*b*) *Indirect Laryngoscopy*

The patient, seated, protrudes his tongue and holds it firmly in a towel, or a small napkin, between his thumb and fore-finger, opening the mouth as wide as possible. By pulling the base of the tongue forward in this way, the epiglottis is lifted. The head is held upright (inclined neither backward nor forward), and the examiner sits close to his patient, the legs of the patient between the knees of the examiner. By means of the head mirror, or, better, a head-light, as broad a light as possible is thrown into the throat. The round laryngeal mirror, somewhat larger than that used in posterior rhinoscopy, is warmed over the lamp, so that moisture will not be precipitated upon it, tested on the back of the hand against over-heating, and then its back is pressed lightly against the uvula so as to hide the latter entirely, it and the soft palate being displaced gently backward and upward in order to supply the necessary space. The handle of the mirror, held in the examiner's hand like a pen, should be kept out of the way by displacing it sidewise to the angle of the mouth. The position of the mirror can be sufficiently varied by rotation of the handle on its long axis, the patient being asked to vocalize, repeating *ah-ah,* in order that the movements of the vocal cords may be studied.

Some patients are so sensitive that the gagging reflex interferes with the examination. Skill, a little patience and reassurance will often overcome this, but it may sometimes be necessary to swab the base of the tongue, the uvula, the soft palate and the posterior pharyngeal wall with a 5-per-cent solution of cocain, the patient being warned to spit out any excess of the solution in order to avoid cocain poisoning.

When satisfactory views of the larynx begin to be obtained, the examination should proceed in an orderly way.

i. General View, and View of the Anterior Parts of the Larynx

It is to be remembered that the *anterior part* of the larynx (*i. e.,* the epiglottis) will appear *above* in the mirror, while the *posterior part* of the larynx (the arytenoid cartilages) will appear at the *lower margin* of the mirror. The *right side* of the larynx will appear in the side of the mirror turned toward the patient's right, and the *left side* in that toward his left.

Usually, one sees first the curved margin of the *epiglottis,* which at the sides goes over into the *aryepiglottic folds.* The region of the *arytenoid cartilages* will be recognized by the projecting nodules (cartilag Santorini) beneath the mucous membrane, lateral from which are nodules formed by the cartilages of Wrisberg. On good illuminat can next make out, lower down, the white *vocal cords,* especial posterior parts. They become wider apart during inspiration, a together during expiration. To get the overhanging epiglottis way, so as to see the cords in their whole extent, as far forw

anterior commissure, one asks the patient to say "Ah-h-h" or a long-drawn-out, high pitched "Hay." During *phonation,* the vocal cords come close together, in the middle line, and become visible throughout their whole length and surface. In this position, one notes the *general appearance* of the structures, the *respiratory mobility* of the vocal cords and of the arytenoid cartilages, the prompt and equal *approximation of the cords* in the

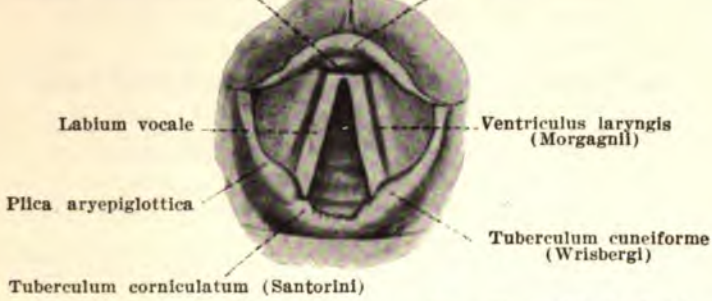

Fig. 140.—Indirect Laryngoscopic View of the Larynx from Above with the Epiglottis Raised and the Glottis Open. (After P. Krause, "Lehrb. d. klin. Diagnostik," published by G. Fischer, Jena.)

middle line on vocalizing, the *color* and *blood supply* of the vocal cords and of other visible parts, and the presence or absence of *scars, ulcers, tumors,* etc.

ii. View of the Posterior Wall of the Larynx

In order to examine the posterior wall of the larynx, and the trachea as far as its bifurcation, the patient sits higher, or stands up, and bends his head well forward, until the chin touches the manubrium sterni. The examiner sits, or kneels, in front of the patient, and looks almost vertically upward at the mirror held horizontally in the patient's throat. The illumination must be good. One sees the *tracheal rings* (perspectively shortened), and sometimes, in the depth, a whitish sagittal ridge, the *bifurcation spur,* and, on each side, the opening into a *bronchus.*

On examining the *posterior* wall of the larynx, in the *interarytenoid region,* the mirror is held a little further forward in the throat than ordinarily (method of Killian).

iii. Lateral View of the Interior of the Larynx

This is best obtained by the method of Avellis. Thus if one wish to examine the left side of the larynx, the patient bends his head to the right, and the back of the mirror is placed against the right side of the soft palate; one can get a good view of the edges of the left false cord and the

left vocal lip, and, on phonation, can sometimes see the floor of the ventricle of Morgagni.

For the pathological findings on laryngoscopic examination, see Special Diagnosis of Diseases of the Larynx.

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3. Bronchoscopy

The technic of the direct examination of the larger bronchi *choscopy*), as worked out by Killian and by Chevalier Jackson, co the introduction of straight, metal, fenestrated tubes, through the

into the larynx, and through it into the trachea, after thorough cocainization of the parts; in children, or in neurotic persons, general anesthesia may be necessary. The tubes have a diameter of 7-10 mm. for adults, or of 5-6 mm. for children. The outer wall of the tube carries a centimeter scale. The tubes for adults measure 30-45 cm. in length; for children, 15-25 cm. The illumination can be made with a panelectroscope.

Technic.—The fasting patient sits (or lies) with his head thrown far back. The base of the tongue is drawn forward and downward, and the warmed and lubricated tube is introduced into the larynx. During an inspiration, it is passed gently through the glottis. It is then passed cautiously deeper down, the head of the patient now being brought a little more forward. If one of the wider, shorter tubes is passed in first, narrower and longer ones, for examination of the deeper parts, can be shoved in through it. With some practice, it is possible to view the bifurcation of the trachea, the entrance into the two chief bronchi, and, also, by passing the tube into the right or left bronchus, the subdivision of a main bronchus into bronchi of the second order may be brought into view. The same apparatus can be used for esophagoscopy, and for gastroscopy. Hooks, forceps, and cutting instruments can be passed through the tubes for the removal of foreign bodies, the dilatation of a stricture, the removal of a polyp, the excision of a particle of tissue for diagnosis, etc. Only experts can be expected to use the apparatus, but the general practitioner, knowing of the method, can call in such an expert, in case of need.

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C. Examination of the Lungs and the Pleurae

In studying, clinically, the condition of the lungs and of the pleurae, we use the methods of inspection, thoracography, spirometry, palpation,

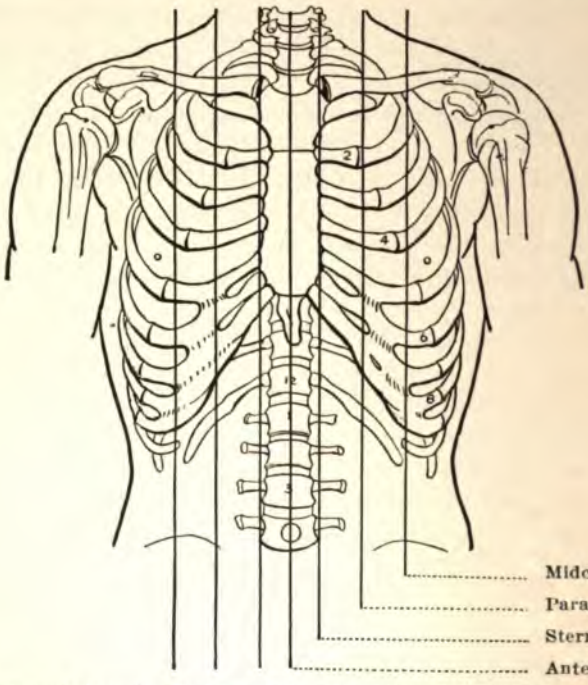

Fig. 141.—Diagram of Anterior Surface of the Chest, Showing Bony Landmarks and Lines Referred to in Descriptions of Topography.

mensuration, percussion, auscultation, x-ray examination, examination of the sputum, and exploratory puncture.

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1. Inspection of the Thorax in Relation to Diseases of the Lungs and Pleurae

(*a*) *Forms of Thorax*

The two forms of thorax of especial importance in this connection are: (1) the extreme expiratory type of thorax, or thorax paralyticus; and (2) the extreme inspiratory, or emphysematous type.

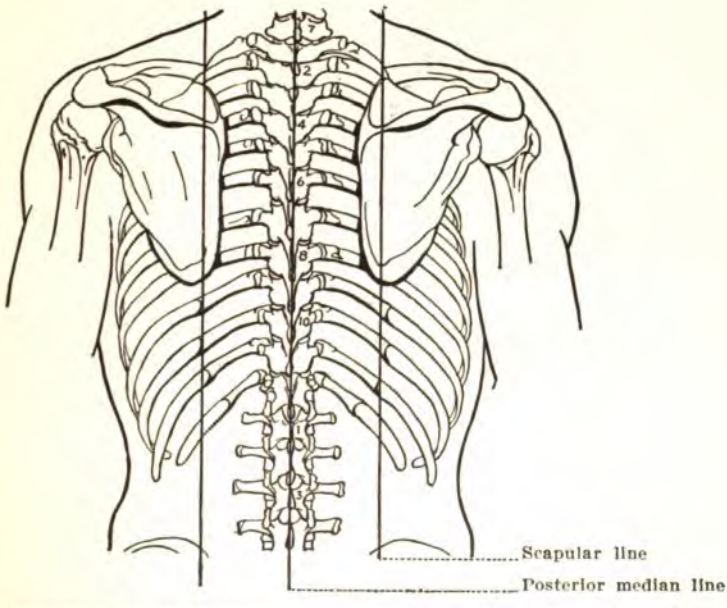

Fig. 142.—Diagram of Posterior Surface of the Chest, Showing Bony Landmarks.

i. Thorax paralyticus or Flat Chest

The extreme *expiratory type of thorax* is easily recognized by (a) its flatness; (b) the absence of the normal projection forward of the sternum and anterior wall of the chest; (c) the short anteroposterior diameter; (d)

the wide intercostal spaces; (e) the low position of the arches of the ribs, separated from the crest of the ilium by only one or two fingers' breadth; (f) the prominent clavicles, with deep supra- and infraclavicular fossae; and (g) the prominent angles of the ribs behind, with lateral displacement of the winglike scapulae. In some instances there is a deep cuplike or funnel-shaped depression known as "funnel chest."

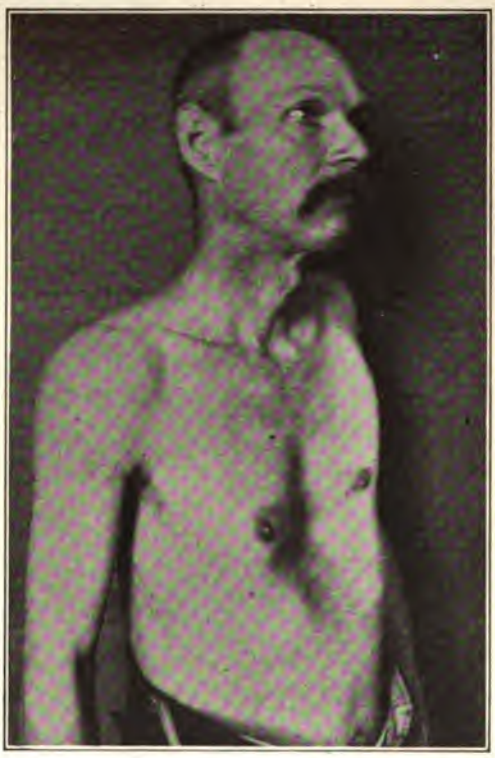

Fig. 143.—Funnel Chest in a Man with Expiratory Type of Thorax—Thorax paralyticus. (Med. Service J. H. H., Photograph by Dr. John Hewetson.)

This form of bilateral contraction of the thorax, usually present from birth, or acquired in early childhood, strongly predisposes its owner to pulmonary tuberculosis.

ii. Barrel-shaped or Emphysematous Thorax

The extreme *inspiratory type of thorax* is just the opposite of the preceding, being characterized by (a) its general fullness; (b) the marked projection forward of the sternum, and of the anterior parts of the chest; (c) the long anteroposterior diameter; (d) the narrow intercostal spaces; (e) the high position of the arches of the ribs, and the great distance between the rib-margins and the iliac crests; (f) the high position of the clavicles and the shortness of the neck; and (g) the bulgings in the supra- and infraclavicular fossae.

This type of thorax appears to be acquired in persons that have for one reason or another (bodily over-exertion, bronchitis, etc.) been compelled to inspire excessively; it is most marked in pulmonary emphysema.

Other deviations from the normal in addition to the two mai described include: (1) the *alar* or *pterygoid chest* (small capacity; a lae projecting like wings); (2) the *transversely constricted chest* (of xiphoid known as "Harrison's groove"); (3) the *pigeon brea natum* (thorax triangular in cross-section; sternum projects fo straightened in front of their angles); and (4) the *rickety chest*

groove on each side, nearly parallel with the sternum; "rickety rosary" at junctions of ribs and costal cartilages).

iii. The Normal Thorax

The two sides are symmetrical; the respiratory movements are equal and contemporaneous on the two sides.

(*b*) *Asymmetry of the Thorax in Relation to Diseases of the Lungs and Pleurae*

While the normal thorax is symmetrical and the two halves participate equally in the respiratory movements, an asymmetrical form of movement is not uncommon in pulmonary or pleural disease. One side may be either pathologically expanded or pathologically contracted.

i. Pathological Expansion of One Half of the Thorax

This may be due to the presence of air, or of fluid, in one pleural cavity (pneumothorax, pleuritic effusions).

A similar expansion may, in rare cases, be due to tumors within the thorax or in the upper abdomen (*e. g.,* in the liver). In pneumothorax, where the pleural cavity is dilated with air under pressure, there is an accompanying obliteration of the intercostal spaces, and marked displacement of the heart.

When one side of the thorax is pathologically expanded, the respiratory excursions on that side are diminished.

ii. Unilateral Contraction of the Thorax

This is more common than one-sided expansion, and is most often due to retraction of the lung (in cirrhosis pulmonum, in pulmonary tuberculosis, or after pneumonia), or to pleural disease (incomplete expansion of lung after absorption of pleuritic exudate, pleural adhesions).

In unilateral contraction of the thorax, the anterior chest wall on the contracted side looks flattened, and its movements lag behind those of the other side on inspiration; the intercostal spaces are deeper than normal.

The unilateral contractions, due to chronic pulmonary tuberculosis, most often affect the upper parts of the lung, beginning with apical retraction; they are characterized by deepening of the supra- and infraclavicular fossae, by flattening of the upper thorax on one side, and by an increase of the area of the heart in contact with the chest wall with more diffuse pulsation and with an apex beat displaced upward and lateralward. Retraction of the lower part of the thorax, on one side, with corresponding displacement of the apex beat, is most often due either to interstitial pneumonia or to chronic pleuritis.

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2. Inspection of the Respiratory Movements

The lungs, during respiration, make no active movements of their own, but simply follow, passively, the movements of the wall of the thorax and of the diaphragm. Two main types of inspiratory expansion of the thorax are seen. In the **costo-abdominal type,** the expansion is due chiefly to the descent of the diaphragm, and less to the elevation of the ribs by the Mm. scaleni, Mm. levatores costarum and Mm. intercostales (*masculine type of breathing*). In the **costal type,** the opposite is the case, the expansion being due chiefly to elevation of the ribs (*feminine type of breathing.*)

The diminution in size of the thorax during expiration depends normally upon the elasticity of the lungs and ribs, not upon muscular contraction.

The times occupied by inspiration and expiration, respectively, are approximately equal, and there is no pause between the two.

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(*a*) *The Diaphragm Phenomenon* (*Litten's Sign*)

In emaciated adults, the respiratory movements of the lower margin of the lung can sometimes be observed as a furrow, descending during inspiration over the intercostal spaces, especially in the lower right thorax (*Litten's sign*). This is due to the separation of the diaphragm from the thoracic wall when it contracts; before the lung can follow it, the atmospheric pressure causes a depression of the soft parts. In children, *Harrison's groove* arises from the same cause, and corresponds to the middle position of the diaphragm.

To observe Litten's sign, the patient is best examined in a room that receives light from only one window, the other windows being darkened. The patient lies with his feet toward the window, the examiner standing three or four steps to one side, at an angle of about forty-five degrees, his back toward the window; the lower part of the thorax, between the axillary and the mammillary lines, is then closely watched. When the movement is visible, linear shadows, interrupted by the ribs, travel down and up during inspiration and expiration respectively; they are easily visible at the level of the sixth or of the seventh rib. These shadows travel over two or three intercostal spaces.

Litten's sign disappears in inflammatory diseases of the lung and pleura, to reappear in convalescence; it may also be absent when the descent of the lung is prevented by pleural adhesions.

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Also, transl.: Province méd., Lyon, ***1895,*** *ix, 278–281.*
Das Zwerchfellphänomen und seine Bedeutung für die klinische **Medicin.** *Wien. klin. Wchnschr.,* ***1895,*** *viii, 79–81.*
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(*b*) *Frequency and Rhythm of the Respirations*

The number of breaths taken by healthy adults varies between 16 and 20 per minute; in the new-born, it averages 44 per minute. The normal relation between respiration rate and pulse rate is as 1:3½, or as 1:4.

The rate in disease may be increased or decreased.

Increase of the frequency of respiration **(tachypnea)** is met with (1) most diseases of the respiratory system (pneumonia, pleurisy, pulmona tuberculosis, emphysema, pneumothorax); (2) in many diseases of t heart; and (3) in those diseases of the abdomen that hinder the mo ments of the diaphragm (ascites, abdominal tumors, peritonitis). tachypnea, the number of respirations may reach 40, 60, or more, p minute, and the relation between respiration rate and pulse frequen changes from 1 : 4 to 1 : 2. In certain diseases of the nervous syst (vagal attacks, hysteria), excessive tachypnea (60 to 80 respirations p minute) may occur in paroxysms.

Slowing of the respiration **(bradypnea)** may be met with (1) in af tions of the brain or of its membranes (increased intracranial pressu (2) in irritations of the respiratory center in the medulla; (3) in se infections; (4) in uremia; and (5) in the death agony. A special form pathological bradypnea is met with in diabetic coma, where the respirati though slow are loud and deep (large breathing, or **air hunger** of Ku maul).

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i. Cheyne-Stokes Breathing

In this form of respiration, periods of complete cessation of the r spiratory movements (*apnea*) alternate with periods in which the respi tions slowly increase in frequency and volume to a maximum, and th again decrease until they cease. During the apneic phase, the patie are sleepy, and the pupils are contracted and non-reactive; as the resp atory movements return, the psyche awakens, and the pupils dilate a again become responsive. The phenomenon is met with, most often, i in cardiorenal cases (uremia, decompensation); (2) in extensive arte sclerosis, especially when the cerebral vessels are involved; and (3) severe lesions of the brain (apoplexy, embolism, brain tumor, men abscess).

The behavior of the blood pressure in Cheyne-Stokes breathing interesting. (See Harvey Cushing's article.)

A slight periodicity to the breathing, somewhat resembling the Stokes rhythm, may be met with in health during sleep; in babies and in old age, the resemblance may be very close.

In meningitis the so-called *meningitic breathing*, or Biot's br is sometimes observable and is of grave omen. The respiratory r

are very long (5-30 seconds or more), in periods which may recur more or less regularly or wholly irregularly.

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ii. Dyspnea

Healthy persons, while at rest, breathe quietly and easily. Any condition, however, that increases the carbon dioxid content of the blood leads to acceleration and deepening of the respirations. This is seen normally on exercise, and in disease either of the lungs or of the circulatory apparatus it may become very marked, causing shortness of breath (*dyspnea*). According to the phase of the respiratory process in which the difficulty of breathing appears, we distinguish an inspiratory type, an expiratory type, and a mixed type of dyspnea.

In the **inspiratory type,** the ordinary muscles of inspiration (diaphragm, external intercostals, scaleni) undergo exaggerated contraction, and, in addition, three other auxiliary groups of inspiratory muscles are called into play: (1) those expanding the thorax by lifting the ribs (M. serratus posterior superior and M. sternocleidomastoideus); (2) those relieving the thorax of the weight of the upper extremities (M. trapezius, M. levator anguli scapulae, M. rhomboideus major and minor); and (3) those that help to expand the thorax when the shoulder girdle is fixed by the activity of the preceding groups (M. serratus anterior major, M. pectoralis major, M. pectoralis minor). When all three groups are active, the patient sits up in bed, with his head, arms and thorax held rigid, panting for breath;

the condition is known as **orthopnea.** In marked dyspnea, the extensors of the spine, the muscles that dilate the nostrils, and those that open the mouth and larynx are also active. In the highest grades of inspiratory dyspnea, one can observe an *inspiratory retraction* over the xiphoid cartilage and over the lower ribs, especially when the dyspnea is due (1) to stenosis of the larynx, trachea or bronchi, (2) to a diffuse capillary bronchitis, or (3) to an extensive pneumonia.

In the **expiratory type** of dyspnea, it is the contraction of the thorax that is faulty, and the duration of expiration becomes longer than that of inspiration. Instead of the normal contraction, due to elasticity, certain expiratory muscles become active, especially the abdominal muscles and the M. quadratus lumborum. Bronchospasm is often an important factor in the origin of an expiratory dyspnea.

Expiratory dyspnea is met with especially in pulmonary emphysema, where it is permanent, and in bronchial asthma, where it is paroxysmal.

The term **asthma** is used to designate paroxysmal dyspnea. One distinguishes nervous or bronchial asthma (*asthma bronchiale*) from the paroxysms of dyspnea that occur in cardiac disease (*asthma cardiale*), usually due to temporary paralysis of the left heart, and those in renal disease (*asthma uremicum*), which are toxic in origin, not to be confused with the cardiac asthma due to myocardial insufficiency that may accompany the nephropathy.

Mixed dyspnea, in which both inspiration and expiration are more difficult than normal, is met with in most affections of the lungs and pleurae that diminish the respiratory surface or limit the respiratory movements. Mixed dyspnea is also met with in circulatory diseases. Here, the diminished velocity of the blood in the pulmonary vessels leads to disturbance of gas exchange; and this is further complicated by the structural and functional changes in the alveolar epithelium in chronic passive congestion.

Recent studies on dyspnea show a close relation of the stimulation of the respiratory center to acidosis. One of the best methods of determining the degree of an acidosis is to measure the *carbon dioxid tension in alveolar air* (Porges, Leimdörfer and Markovci). A decreased alkalinity of the blood such as is met with in acidosis is accompanied by a corresponding decrease of the carbon dioxid tension in the blood, and this is associated with a decreased carbon dioxid tension in the alveolar air.

The alveolar air can be obtained for examination by the method of Haldane and Priestley, or by the simplified methods of Boothby and Peabody, of Ple Higgins, or of Roth, the air collected being analyzed in the laboratory by of Haldane's small type of air analysis apparatus.

Less exact analyses, but probably sufficient for clinical purposes, can l by the very simple method described by Fridericia.

Since Hasselbach showed that an increase in the irritability of the r centers will induce a lowering of the carbon dioxid tension, such studies come of still greater clinical interest.

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3. Determination of the Volume of the Inspired and of the Expired Air (Spirometry)

The measurement of the air entering and leaving the lun phase of respiration can be made by means of a **spirometer**.

The apparatus originally used was that of Hutchinson (1846); a ment is that devised by Tissot (1904). More recently, Plesch's m

the apparatus of Bohr has come into use. For the determination of the residual air, either pneumotometric methods (Hartesz, Gad, Pflüger) or gas-mixture methods (Davy, Allen and Pepys, Durig, Plesch) can be used. As these methods are applied only in research work, it does not seem desirable to give the details of the technic in this treatise.

Certain terms in connection with spirometry should be understood. By **vital capacity** is meant the amount of air that, after the deepest possible inspiration, can be expelled on full expiration; it averages in healthy men 3,600 c.c., varying from 3,000-4,000 c.c.; in women it averages 2,500 c.c., varying between 2,000-3,000 c.c. The value depends upon the height of the body, each centimeter of height in the adult corresponding to 22 c.c. of expiratory air. This vital capacity is smaller in childhood and in old age, as well as in all diseases of the respiratory system. The stomach should be empty when the test is made.

By **complementary air** is meant the amount that, after a quiet inspiration of normal depth, can be taken in by the most forcible inspiration. It amounts to about 1,500 c.c. By **reserve air** is meant the amount that, after the normal quiet expiration, can still be expelled by extremely forcible expiration (1,500 c.c.). By respiratory **breathing air** is meant the amount that is taken in, and given out, on quiet respiration (500 c.c.). By **residual air** is meant the amount that remains in the lung, after the deepest possible expiration (800 to 1,600 c.c.).

The sum of the complementary air, the reserve air and the breathing air, therefore, corresponds to the *vital capacity*, which is measured by the spirometer; the *total lung capacity* is this sum plus the residual air; the *mean capacity* is the sum of the residual and the reserve air. The amount of air taken in during a minute on quiet respiration varies from 5-7 liters.

The vital capacity of the lungs enlarges on bodily exercise and in pathological states accompanied by dyspnea; the latter is a compensatory process, the temporary pulmonary emphysema (a sort of physiological reflex [Bohr]) favoring an easier and quicker circulation of the blood through the pulmonary blood vessels.

It looks now as though studies of vital capacity may turn out to be of distinct value in clinical diagnosis (F. W. Peabody).

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4. Thoracography or Pneumography

The alterations in the circumference of the whole thorax or of one half of it can be registered in the form of respiratory curves, so that changes in the frequency, rhythm, extent and course of the respiration can be more exactly studied. A very good instrument for clinical work is that of Marey. Various modifications (Brondgeest, Ochnike, Knoll) are in use.

Still more exact instruments are used in research work (Stethometer of Gibson, Recording Stethometer of Burdon-Sanderson, Thorakographs of Fick, Levy-Dohrn, and P. Bert). Such instruments and the technic of using them are described in F. Schenck's article in Tigerstedt's Hdb. d. physiol. Technik, Leipzig, 1911, II.

A normal pneumogram is shown in Fig. 144. Expiration is perhaps a trifle longer than inspiration and there is a very brief pause between.

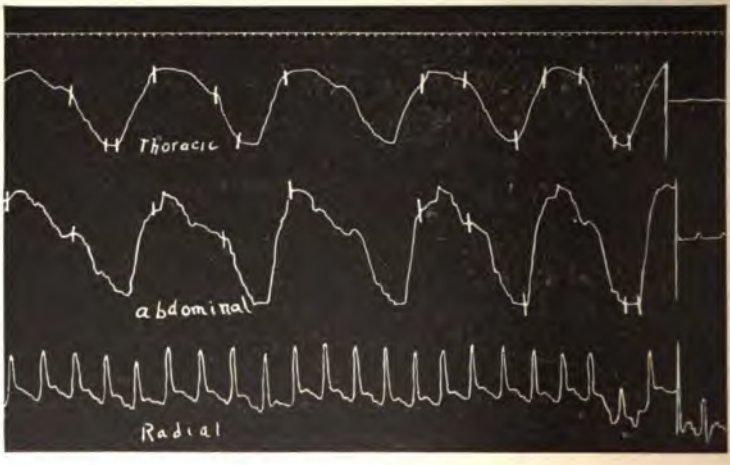

Fig. 144.—Normal Pneumographic Tracing or Pneumogram. The Curve Shows Transmitted Vascular Pulsations. Inspiration 0.8 Sec.; Inspiratory Pause 0.3 Sec.; Expiration 0.9 Sec.; Expiratory Pause 1.3 Sec. (Med. Service, J. H. H.)

In *normal breathing*, inspiration proceeds quickly and evenly as a result of contraction of the muscles of inspiration. The ascending limb of the pneumographic curve therefore shows an even inspiratory course. When expiration begins, the curve descends quickly at first, but a little more slowly toward the end before the expiratory pause is reached. The form, extent and frequency of the respirations of the normal man while awake are tolerably constant, but in pathological states

any one of these features may be altered. Thus, in *orthopnea,* the conditions are such that the inspiration may still be easy, though expiration is difficult, owing to depression of the normal elastic forces of respiration. On sitting up, the diaphragm is displaced some distance caudalward; this separation of the diaphragm from the center of the thorax causes a stronger tension of the lungs and thus facilitates expiration. Furthermore, the muscles of the abdominal wall can aid more in expiration when the patient is sitting up.

The general disturbances of the *form* of respiration have been carefully described by L. Hofbauer. These may involve changes in inspiration, in expiration, or in the expiratory pause.

Inspiration may be prolonged in diseases of the air passages (tracheal stenosis, croup, edema glottidis, whooping-cough, bronchostenosis). Prolongation is also

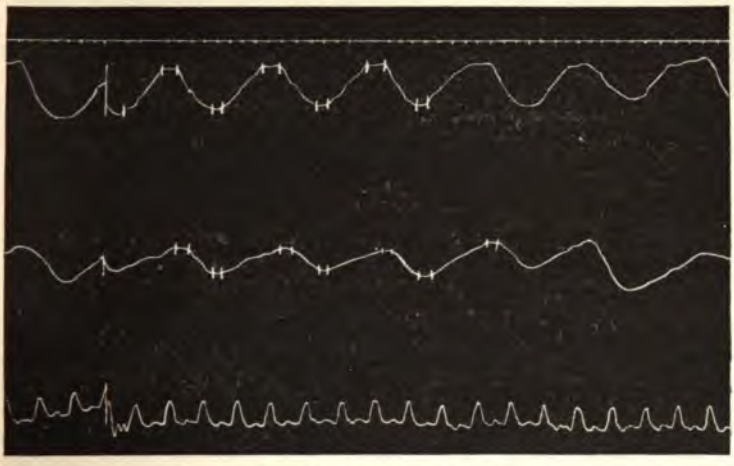

Fig. 145.—Pneumogram in Pneumonia. Inspiration 0.4 Sec.; Expiration 0.6 Sec.; Pause 0.4 Sec. (Med. Service, J. H.)

met with in diseases of the lungs (croupous pneumonia, lung abscess, lung gangrene, pulmonary tuberculosis), in the cardiac asthma of heart disease, in uremia and in diabetic coma.

Inspiration may be shortened in the air hunger of uremia, though it is lengthened in the air hunger of diabetic coma.

Flattening of inspiration is always associated with prolongation of inspiration, and deepening of the inspiration is met with in all cases of air hunger (both uremic and diabetic).

Expiration is prolonged in tracheal obstruction from foreign bodies, in polypi beneath the glottis, in bronchial asthma, in cardiac asthma, in mediastinal tumor, in pericarditis, and in many cases of chronic circulatory insufficiency. The same is true in pleuritis and in most diseases of the lung.

Expiration is shortened in uremia during the stage of air hunger; a shortening of expiration has also been observed in cardiac decompensation and in the asthma of Graves' disease.

The so-called "active expiration" due to muscular contraction (in addition to the normal expiration due to elastic forces) is accompanied by prolonged expiration; it is met with in bronchial asthma, in pleurisy, in pneumonia, in pneumothorax, and in tumors of the mediastinum and of the pleura. A similar active expiration

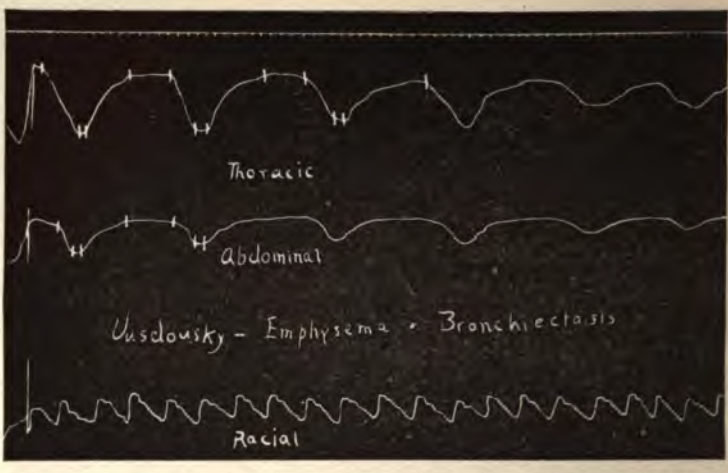

Fig. 146.—Pneumogram in Emphysema with Bronchiectasis. Inspiration 0.6 Sec.; Inspiratory Pause 0.3 Sec.; Expiration 1.1 Sec.; Expiratory Pause 0.8 Sec. (Med. Service, J. H. H.)

has been observed in cerebral diseases and in nephritis. One can sometimes recognize active expiration in the pneumographic curve by the disappearance of the terminal flattening of the curve; in other cases, it is manifested by the intercalation of a steep portion in the expiratory curve (normally parabolic).

The *expiratory pause* is prolonged in the air hunger of uremia, in the asthma of Graves' disease, and in certain focal diseases of the brain (especially in tumor or abscess of the cerebellum, and in cerebral hemorrhage).

The expiratory pause is shortened in all cases of tachypnea, as in the ordinary asthma of Graves' disease and in hysterical tachypnea; it is also shortened in all

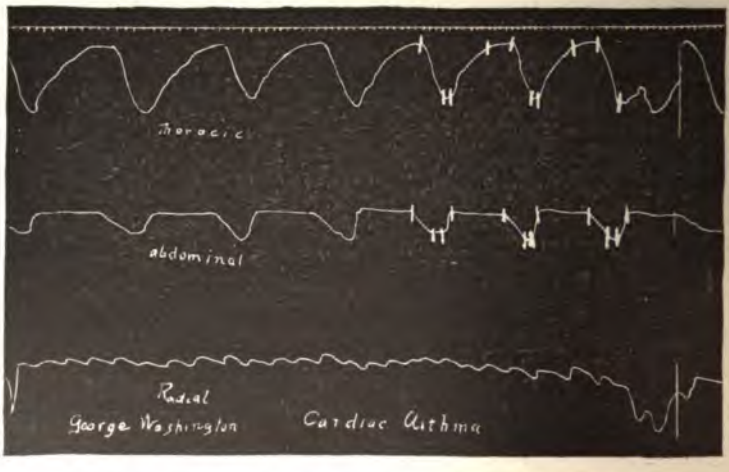

Fig. 147.—Pneumogram in Chronic Circulatory Insufficiency (Cardiac Asthma). Inspiration 0.8 Sec.; Inspiratory Pause 0.2 Sec.; Expiration 1.4 Sec.; Expiratory Pause 0.8 Sec. (Med. Service, J. H. H.)

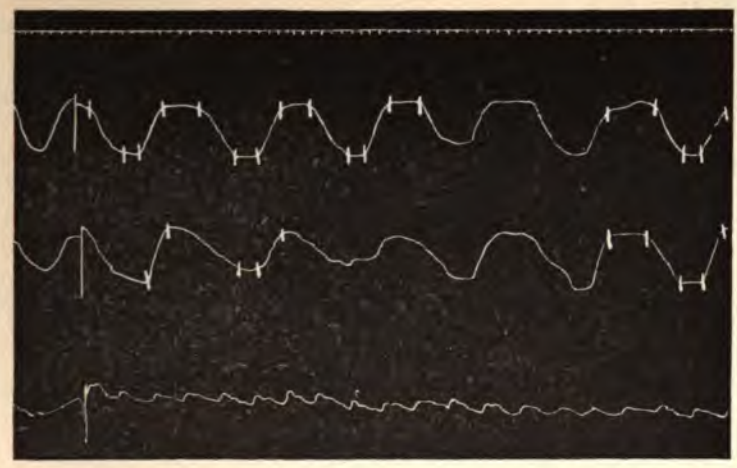

Fig. 148.—Pneumogram from Patient with Ascites. Inspiration 0.8 Sec.; Inspiratory Pause 0.4 Sec.; Expiration 0.4 Sec.; Expiratory Pause 0.8 Sec. (Med. Service, J. H. H.)

cases in which the individual respirations are prolonged (pneumonia, pleurisy, pneumothorax).

For full descriptions of other disturbances of the pneumographic curve and for the changes met with in individual diseases, the excellent article by Hofbauer may be consulted.

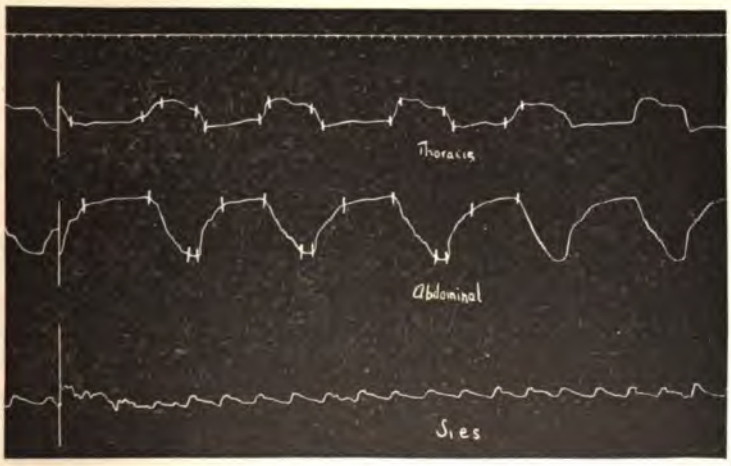

Fig. 149.—Pneumogram Illustrating Paradoxical Breathing in a Patient Suffering from Severe Renal Disease. Compare the Abdominal with the Thoracic Curve. Inspiration 0.8 Sec.; Expiration 0.6 Sec.; Expiratory Pause 0.8 Sec. There was "Active Expiration." (Med. Service, J. H. H.)

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5. Palpation of the Thorax Over the Lungs and the Pleurae

A most important part of the palpation of the thorax is the testing of the vocal fremitus, the tremor of the voice propagated to the thoracic wall through the bronchi and pulmonary tissue. The test is made by placing the two hands on symmetrical portions of the thoracic wall and asking the patient to repeat in a loud deep voice ("1, 2, 3," "99"). In health, the vocal fremitus may be a trifle more marked on the right than on the left side, owing to the greater diameter of the right bronchus. It is feebler when the voice is weak and of high pitch (especially in women). If a patient be asked to sing the scale, the fremitus will be found most marked at one of the lower notes, a level corresponding to the resonance of the lung. In women, the tone-level of the voice is usually higher than the resonance of the lung, so that the latter is not aroused to sympathetic vibration (F. Müller).

As a clinical method, palpation of the vocal fremitus has approximately the same value as auscultation of the respiratory murmur; sometimes it is a more delicate test, especially in deciding whether a dullness over the lower thorax is due to infiltration of the lung or to pleural effusion; an increased vocal fremitus indicates better conduction from the larynx to the lung surface (infiltration), while an enfeeblement or an abolition of the fremitus suggests pleural effusion or pneumothorax. Certain exceptions to this rule should, however, be noted. In massive pneumonia, with plugging of the bronchus, the propagation of the voice may be temporarily interfered with; again, in pleural effusion, there may be less diminution of the vocal fremitus than might be expected because pleural adhesions, uniting the lung to the wall of the thorax, may favor the conduction of the voice-tremor, or an atelectasis, due to the pressure of the exudate, may increase the vocal fremitus more than the effusion weakens it (D. Gerhardt).

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6. Mensuration of the Thorax

By passing a tape around the chest, just above the nipples, the arms being held out from the sides, we measure the *circumference of the chest.* On physical examinations for entrance to the army, navy, etc., this value is used as a measure of the development of the thorax, and serves as a clew to the general constitution of the person. In healthy young men, the circumference should exceed 80 cm.

More important as regards the state of the lungs themselves is the *difference in circumference on deep inspiration and on deep expiration.* Normally, this difference amounts to about 7 cm. (extremes 5-7 cm.).

The *sternovertebral diameter,* measured by calipers from the manubrium to the back, in a horizontal plane, amounts to 16 cm.; from the lower end of the corpus sterni to the back, it amounts to 19 cm. The *transverse diameter* (diameter costalis), at the level of the nipples, measures about 26 cm.

The comparison of the *circumference of each of the two halves* of the chest shows normally a difference of ½-2½ cm., in favor of the right side. In an asymmetrical thorax, due to unilateral expansion or retraction, exact measurement is important for the record, though, for the actual recognition of the asymmetry, experience teaches that slight differences in circumference of the two halves of the chest can be more easily recognized by careful judgment with the eye than by mensuration.

Exact records of the form of the thorax can be made with a *cyrtometer.*

7. Percussion Over the Lungs and Pleurae

Percussion.—By percussion, we produce sounds that permit us to draw conclusions regarding the structure of the organs beneath the part percussed. The shock given by the percussion stroke gives rise to sounds that vary with the elasticity (capacity for vibration) of the parts struck; the greater the elasticity, the more marked is the sound production.

Historical.—The method of percussion was first devised by L. Auenbrugger (1761). It became generally known and applied to the study of the heart through Corvisart (1808). It reached its flower when it was applied in a most thorough way to the diagnosis of diseases of the lungs by Laennec (1810). These clinicians all used DIRECT PERCUSSION, producing sounds by simply tapping the surface of the thorax with the finger tips of one hand. INDIRECT PERCUSSION was devised by Piorry (1826), a *plessimeter* being intercalated between the chest wall and the percussing fingers; and, later, Wintrich (1841) substituted a *percussion hammer* for the percussing fingers.

Principles of Percussion.—Airless bodies enter into sound-producing vibration only when they are rigid, or in a certain state of tension. In the human body, bones alone correspond to such a state, but even they are surrounded by soft parts, so that they are not reached by the percussion

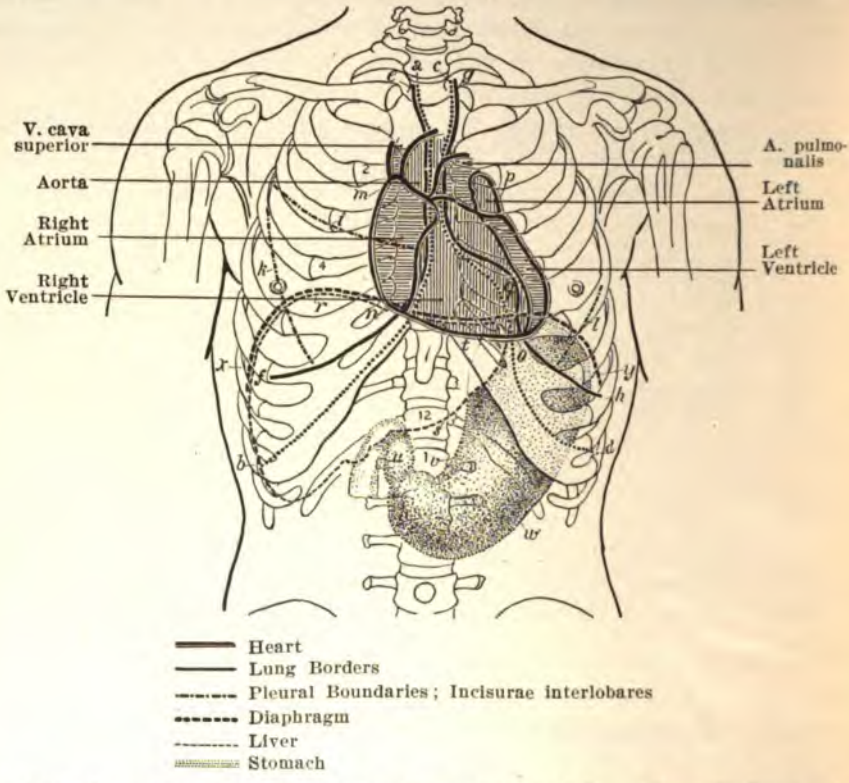

Fig. 150.—Topography of the Thoracic and Upper Abdominal Viscera from in Front. a-b—Boundary of Right Pleural Cavity; c-d—Boundary of Left Pleural Cavity; e-x—Edge of Right Lung; 9-h—Edge of Left Lung; i—Upper Incisura lobularis (Right Lung); Lower Incisura lobularis (Right Lung); l—Left Incisura lobularis; m-n—Right; n-o—Lower; p-o—Left Border of Heart; q—Mediastinal Sinus Situated Between the Pleural Boundaries and the Incisura cardiaca of the Anterior Edge of the Left Lung; r—Highest Point of the Liver, Overlapped by Lung; s—Lower Edge of Liver; t—Pars cardiaca; u—Pars pylorica; v—Lesser Curvature; w—Greater Curvature of the Stomach.

stroke, or, if reached, transfer their vibrations to adjacent vibrating (because air-containing) soft parts, and so are less responsible than t[illegible] for any sounds produced.

The sounds yielded by soft parts when percussed depend u[illegible] air (or gas) content (Skóda). If the air or gas be contained cavities, it is set into vibration, and along with it the wall of the started vibrating to a greater or less degree; if the air be dist the form of small alveoli throughout the whole tissue, as in th[illegible]

air and the tissue vibrate together on percussion. Obviously, then, percussion permits us (1) to find the limits of juxtaposed airless and air-containing structures, and (2) to form judgments regarding (a) the air content, and (b) the degree of tension of air-containing organs.

Direct Percussion.—This is but little used nowadays, perhaps less than it should be. It is valuable for quick orientation (1) regarding the

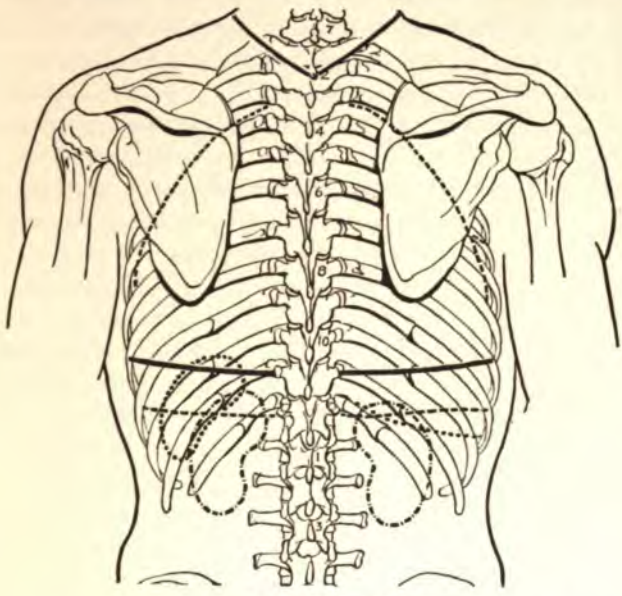

Fig. 151.—Topography of the Viscera, Viewed from Behind.

comparative state of the two sides of the lower thorax behind, and (2) regarding the position of large areas of infiltration (pneumonia, tuberculosis), or of large pleural effusions.

One arranges the finger tips of the right hand in a plane and, to produce the sounds, delivers the stroke directly upon the surface of the thorax, without any intermediary plessimeter.

Indirect Percussion.—In this method, the blow, instead of being struck directly upon the body surface, is delivered upon some intermediate body placed upon the part under study. This intermediate body is called a PLESSIMETER or pleximeter. As a plessimeter, we may use the index, or the middle finger, called a "plessimeter-finger," or, instead, a platelet made of rubber, gutta-percha, ivory, glass or metal. To ascertain the condition of the structures behind the clavicle, we often use the clavicle itself as a plessimeter.

The *advantages of a plessimeter* lie in the facts that by means of it (1) the percussion stroke can be made to reach to a greater depth on the one hand, and (2) it can be applied to a smaller surface area on the other. Lack of compressibility and the greatest possible elasticity are desiderata in a plessimeter, since, when an elastic plessimeter is struck, the hammer or the percussing finger rebounds from it before the underlying parts are pressed in, and there is less of the actual energy of the percussion stroke lost, so that the effect of the percussion extends farther into the depth. Plessimeters of ivory, metal, and glass conform most closely to ideal requirements; soft rubber is just as elastic, but is more compressible, so that the effect of the percussion does not extend so deep and the percussion sound is not so loud.

The *plessimeter finger* is most often used, partly because it is always available, and partly because it permits us to judge of the FEELING OF RESISTANCE, thus yielding most valuable information accessory to the percussion sounds. Moreover, it is possible easily to approximate it to the surface in regions difficult of access to a rigid plessimeter (*e. g.*, intercostal spaces in front, supraclavicular fossae. On the other hand, as regards elasticity and compressibility, the finger is far inferior to an ivory plessimeter.

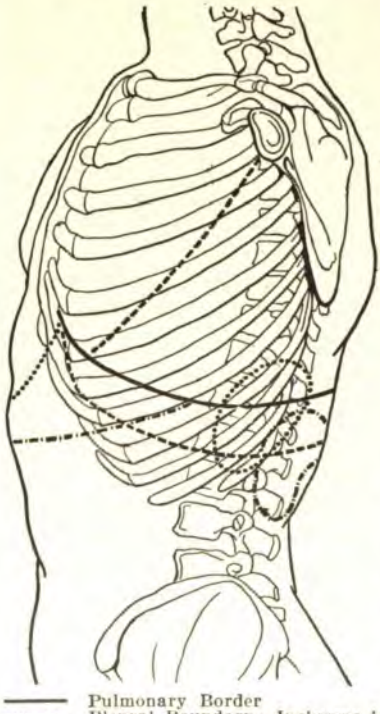

Fig. 152.—Topography of the Thoracic and Upper Abdominal Viscera, Viewed from the Left Side.

As a PERCUSSOR, or PLESSOR, it is customary in America to use the *middle finger* of the right hand, flexed to an obtuse, or almost a right, angle at the terminal joint, and slightly flexed at the proximal joint of the finger. The stroke is delivered entirely from the wrist, the forearm remaining in position. With practice one soon learns how best to deliver the stroke, gently for "superficial percussion," more forcibly for "deep percussion." As a rule, the percussing finger should be allowed to rebound immediately from the pl eter after it has struck, in order t plessimeter may freely vibrate with the part beneath. In some i it may be desirable more or less to dampen the vibration by the each side of the plessimeter finger, or, again, one may use

in succession as plessimeter fingers, passing quickly from one to another. In *gentle percussion*, the plessimeter finger should lie merely in smooth contact with the part under study; for *deep percussion*, it may be firmly pressed against this part. Many clinicians, especially in Europe, make use of a *percussion hammer*, the head of which is covered with hard rubber, leather, or felt (to avoid the production of a tone dependent upon the hammer and the plessimeter themselves, and masking the sound produced by vibration of the underlying organ).

Fig. 153. — Goldscheider's Orthopercussion. (After A. D. Hirschfelder, "Diseases of the Heart and Aorta," published by J. B. Lippincott Co., Phila.)

In *orthopercussion*, the force of the blow is directed exactly perpendicular to the surface. (Figs. 153 and 154.)

The STRENGTH OF THE PERCUSSION STROKE should vary greatly according to the conditions of the examination. When the soft parts over the organ under examination are thick, the stroke must, of course, be harder to set that organ in vibration; otherwise, delicate differences in the intensity of the sound produced are more easily perceived when the sound is not loud. Thus, in determining the so-called SUPERFICIAL OR ABSOLUTE DULLNESS of the heart, or of the junction of an air-containing organ with an airless part (lung limits), *feeble percussion* should be employed. For this purpose, the NO-SOUND STROKE, as described by Henry Lee Smith, is very helpful; the strength of the stroke is such that no sound at all is produced (just disappears) over an airless area. Passing from this to an air-containing or gas-containing area with the same strength of stroke, a percussion sound is immediately produced as the boundary is passed (lung limits, edge of liver, etc.).

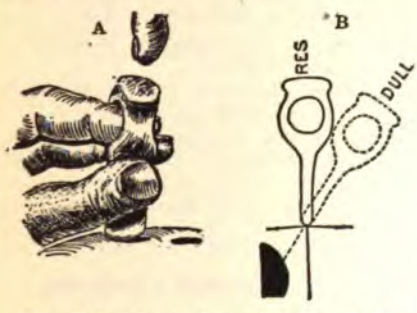

Fig. 154.—Percussion with the Orthoplessimeter. (A) J. O. Hirschfelder's Orthoplessimeter and Its Mode of Application. (B) Supposed Line of Transmission of the Percussion Impulse from the Orthoplessimeter. Res, Resonant Percussion Note. (After A. D. Hirschfelder, "Diseases of Heart and Aorta," published by J. B. Lippincott Co., Phila.)

In the determination of so-called DEEP OR RELATIVE DULLNESS, however (as, for example, the lateral margin of the heart or the upper surface of the liver covered by lung), it is necessary to use a somewhat stronger stroke, though even here one does best to use percussion of *medium force* rather than the very strong percussion so often employed. Goldscheider has shown that the no-sound stroke can also be used for determining the location of the boundaries of deep dullness (so-called *threshold-value percussion*).

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(a) The Intensity and the Quality of the Sounds Produced on Percussion

In the percussion of the thorax, as elsewhere, one pays attention to the following points, regarding the sounds produced:

1. Their *loudness* (loud or feeble, clear or dull).
2. Their *fullness* (full or empty, long or short).
3. Their *pitch* (high pitch or low pitch).
4. Their *clang* or *timbre* (tympanitic or non-tympanitic; cl
or not clang-rich; metallic or non-metallic).

i. The Loudness of the Percussion Sounds

This depends, essentially, upon the amount of air or ga
examined. Airless parts yield only a feeble sound (dul

"thigh sound"). In general, the sound is louder and "clearer," the greater the air content of the organ percussed, though the tension of the walls has some influence upon this (see Tympanitic Sound).

In other words, the terms "clear" and "dull" refer to the *intensity* of the sound. Measurements by means of microphone and galvanometer, as well as by means of the phonograph, have shown that the clear sound, or resonance, of the normal lung corresponds to waves of decidedly greater amplitude than the dull sound (F. Müller). It should be especially noted that the expressions "clear" and "dull" are used, clinically, in a different sense from that of ordinary speech. In the latter, by a "clear note," is usually meant a high clang, and by a "dull sound," a low clang. Clinically, on the contrary, one refers to the *loudness* of the sound, that is, to the *amplitude* of the sound waves that strike the ear drum. This *intensity* depends on (1) the capacity for vibration, especially upon the amount of air in the organ percussed; and (2) the strength of the percussion blow. In comparative percussion, therefore, one should always use exactly the same force, and should especially avoid confirming a preconceived opinion by unequal force of the percussion blows, for unequal force will produce unequal sounds and dullness may thus be simulated.

ii. The Fullness of the Percussion Sounds

The terms "fullness" and "emptiness" have to do mainly, as experiments with the microphone and the phonograph prove, with the *duration* of the sounds, the full sound lasting long, the empty sound being brief. Healthy, air-containing lung yields a full sound (0.42 seconds in length); the solid, infiltrated lung yields an empty sound (0.28 seconds) (F. Müller). The difference in duration is not great, but is distinctly perceptible by the ear.

A percussion sound is *full* (of long duration) when it is rich in low tones, because these tend to die away more slowly (pulmonary emphysema, pneumothorax). The term "empty sound" is not precisely equivalent to "dull (feeble)," though, as a rule, the loud sounds are also full and the dull sounds are also empty (F. Müller).

iii. The Pitch of Percussion Sounds

In the physics of sound, as is well known, the *pitch* of a tone depends upon the number of vibrations per second. The greater the number of vibrations, the higher the tone. From the standpoint of pure physics, percussion sounds are always *noises,* composed of a large number of individual *tones.* In the percussion sounds elicited over the lungs, experiments with large resonators (F. Müller) have shown that the tone series present extends from C down as far as F. The upper limit of this series is unimportant, since it depends, mainly, on the plessor and the plexímeter, but the lower limit is of great significance. The percussion sound over the healthy lung contains lower tones in the adult than in the child; the lowest tones are met with over the distended lungs in pulmonary

emphysema and especially in pneumothorax (even as low as E). When the apex of the lung is infiltrated (*e. g.*, in tuberculosis), low tones are absent over it, though they are still present over the other healthy apex, and the percussion sound is, therefore, said to be of "higher pitch" (better, of "less low" pitch) on the diseased side.

Of all the tones in a series contained in the sounds elicited on percussion of the lungs, the lowest ones tend to be the loudest, and to die away most slowly (being also of longer duration). A percussion sound, therefore, that contains (1) very low tones is usually also (2) loud (—clear) and (3) full (—long-lasting).

The ear should be carefully exercised in the appreciation of the lower tones, especially on percussion. When one tone is dominant, as in tympanitic sounds, the height of its pitch is easily recognizable to one that has a good tone-pitch sense. The recognition of differences in the pitch of the dominant tone in tympanitic sounds lies at the basis of the recognition of the so-called "alterations in pitch," on change of conditions, of Wintrich, Gerhardt, etc. (*vide infra*).

Tympanitic sounds are fuller (*i. e.*, of longer duration) than non-tympanitic sounds, a fact that sometimes helps us to recognize them.

iv. The Clang-content, or Timbre, of Percussion Sounds

The tympanitic sound resembles a clang and usually permits of the recognition of the definite pitch of the fundamental, dominant tone in the clang. A tympanitic percussion sound is met with over large cavities containing air or gas (*e. g.*, over the larynx, the trachea, the stomach, and the intestine). The healthy lung yields a non-tympanitic sound on percussion; in this there is no definite, fundamental, dominant tone. A single exception must be made; over the lower part of the left lung, where we, in reality, percuss over a thin lung-margin, and over the diaphragm, we may elicit the tympany of the underlying stomach.

A typical tympanitic sound can be experimentally produced by percussion over a hollow membranous sphere; thus, if one cut out a stomach and blow it up, it will be found that tympany, on percussion, is most distinct when the walls are under a certain optimal degree of tension. The tympany will become less distinct when the tension is of lower, or of higher, grade. If, after the degree of distention corresponding to the maximal tympany has been reached, the stomach be gradually blown up further, and be tested from time to time, one can convince himself, as the tension of its walls increases, not only that the richness in clang changes, but that there is also a change in the pitch of the sound; as it becomes poorer, or "harder," in clang, the pitch becomes higher; in other words, the percussion sound becomes (1) higher and (2) emptier. Physicists assert that this change in the character of the clang, through the tension of the walls, is due to the fact that both the gas content and the walls are concerned in the production of the sound. The more capable of vibration both are, the easier it is for each to adapt its vibration to that of the other; thus, when the wall is adaptable, the rhythm of the vibrations depends essentially on the size of the cavity; here the "gas dominates the sound

and hence the tone is of low pitch." But if the wall, through its tension, is made incapable of performing slow vibrations, it will then hinder the origin of low tones, even in the gas space; the vibrations of the gas must then adapt themselves to those of the wall; the "wall becomes the dominator of the sound" (D. Gerhardt).

The explanation of tympanitic and non-tympanitic sounds over the lungs is somewhat more complicated than for the simple gas of a large hollow space, such as has just been described. As a matter of fact, the normal lung, *in situ*, yields a non-tympanitic sound on percussion, but the lung removed from the body and percussed yields a tympanitic sound, though it loses the tympanitic clang again if it be artificially blown up. It has been suggested that the collapsed lung is comparable, in its vibratory capacity, to a layer of foam. In both cases there arises, on percussion, a note of such low pitch that it cannot possibly belong to the proper tone of the small alveoli; it seems certain that the many small air-containing alveoli, and the fine fluid- or tissue-membranes separating them from one another, vibrate as a whole, for the low pitch of the sound increases with the size of the piece of lung, or of the foam mass, percussed, the sound being lower in pitch than would correspond to that of a cavity of the same size. The elastic partitions act, therefore, on the vibrating air mass like ballast, slowing the periodic number. If now the conditions be changed so that the elastic partitions no longer vibrate freely like the fine fluid-membranes of a foam-layer, and are unable to adapt themselves to the vibrations of the air space, but have become rigid through the distention of the lung, the capacity of the lung for vibration diminishes. The tympanitic, low-pitched, fundamental tone then gradually disappears, and there remain only tones of higher pitch (as in the over-distended stomach); the sound becomes emptier, and is no longer tympanitic.

A *tympanitic sound over the lung,* except in Traube's space, points to an abnormal condition within the thorax: (1) to smooth-walled cavities (lung cavities, bronchiectatic cavities, abdominal viscera dislocated into the thorax); (2) to a change in the structure of the lung that leads to *loss of the tension of the alveolar walls;* (a) in *atelectasis* of the lung, from bronchial occlusion, or from compression due to high position of the diaphragm, large pericardial effusions, or pleural effusions; (b) in *edema* of the lung; (c) in certain stages of *pneumonia* when the alveolar septa have changed in texture from the inflammation, though the air content is not yet essentially diminished; (3) to *bronchi* (*running in airless tissue*) having a sufficient air content to give rise to a tympanitic note; and (4) to the *trachea behind solid lung tissue* (as, sometimes, in the child's thorax).

Metallic Sounds, or Metallic Clangs.—A *metallic ring* (or amphoric sound) on percussion depends upon the presence of high over-tones accompanying and obscuring a low fundamental tone. It arises in large gas-containing cavities with smooth walls, but the walls must be tense. It will appear in the blown-up stomach (see above), if the distention be sufficiently increased. To grow familiar with this sound, it may be elicited by percussing over the cheek after the mouth has been so strongly distended by air that the tympanitic sound, present on less distention, disappears. It is best brought out, when elicitable over the thorax, by

percussing with the handle of a percussion hammer or with a lead pencil upon the pleximeter (Heubner's method), and listening, with the stethoscope, over an adjacent area, for the metallic ring or bell-like sound. (See also Coin Sound in Pneumothorax.)

A *cracked-pot sound* (or metallic chink) arises, on strong percussion, if air or gas be thereby driven out of a cavity through a narrow opening. The sound may be imitated by clasping the hands loosely together, and striking the back of one of them upon the knee. It can also be elicited by strong percussion of the chest of a healthy, crying baby. Or, if one hold his own mouth slightly open and the cheek much relaxed, sharp percussion (indirect or direct) of the cheek will give rise to the characteristic sound.

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(*b*) *The Feeling of Resistance on Percussion*

A person percussing is able to draw more conclusions from his percussion than is the listening bystander, since, in addition to hearing better, he experiences certain tactile sensations, not accessible to the bystander, which may be of great value in diagnosis. The sense of resistance, felt by the fingers, on percussion varies with the compressibility of the part percussed. The resistance over solids and liquids is great; that over air-containing parts is much less.

Gerhardt illustrates this point by the sensations received by the finger when it percusses a glass filled with a foaming fluid; as long as the fluid is covered by a thick layer of foam, there is a tympanitic sound; when the foam has disappeared, the sound becomes feebler and shorter, and the percussing finger striking the bottom of the glass feels distinctly that the glass has become less vibratory—it feels *harder.* In other words, the more vibratory a body is on percussion, the softer it feels.

It will be seen that the conditions that give rise to feeble and to empty sounds are those in which the sense of resistance also is great, and, *vice versa,* the conditions that give rise to loud (clear) and to long-lasting (full) sounds are those in which the sense of resistance is less. Upon these facts, also, the so-called *tactile percussion* (Ebstein) is based. (See Delimitation of Deep Cardiac Dullness in the Section on Diagnosis of Diseases of the Circulatory Apparatus.)

(*c*) *Topographical Percussion of the Lungs*

Before comparing the percussion note over symmetrical areas of the two lungs, it is best to mark out, by percussion, the borders of both lungs (*topographical percussion*). In delimiting the lung margins, we use

very gentle percussion (finger-finger, or hammer pleximeter); here the "no-sound" stroke (H. L. Smith) and the "threshold-value" percussion of Goldscheider are very helpful. Since the percussion sounds over the healthy lungs are non-tympanitic, are loud (clear), and die away slowly (of long duration, or full), it is easy to mark off their borders, (1) from adjacent solid organs (heart, liver, spleen, muscles, etc.), which yield a feeble (dull) and short (empty) sound, and (2) from gas-containing abdominal organs, since they yield a tympanitic sound. In outlining the lung limits by percussion, the pleximeter should be moved along lines parallel to the long axis of the body. In very exact work, we may resort to (1) the *linear percussion* of Wintrich, in which the pleximeter is held obliquely, on its edge, while we percuss on its surface; (2) to the *finger position* of Plesch (*q. v.*); but these are refinements of technic, upon which I do not lay much stress.

By the determination of the limit of the pulmonary resonance adjacent to a solid organ is meant the finding and marking of the line at which the loud, full, sound of the lung disappears, on feeble percussion, to give place to the completely dull and empty sound of the solid organ.

The Upper Limits of the Pulmonary Resonance on Percussion.—This is, normally, in the same position on the two sides. To determine it the left fore-finger is placed in the supraclavicular fossa, parallel to the clavicle; we then percuss, passing upward and from the side into the neck. The line of the lung margin passes obliquely, from above, downward and forward, to go over into the medial margin of the lung alongside of the sternocleidomastoid muscle and behind the manubrium. It extends for a distance of from 3-4 cm. above the clavicle at the level of the spine of the 6th or 7th cervical vertebra, and, behind, goes over the edge of the M. trapezius obliquely downward and medialward into the posterior medial lung limit at the level of the spine of the second thoracic vertebra.

Krönig's Fields of Pulmonary Resonance at the Apices.—In addition to this medial upper limit of the resonance of the lung, Krönig determines, by percussion, the lateral limit of the lung resonance. The patient sits on a stool, with his head bent forward and his arms hanging loosely by his sides. The examiner, while delimiting the medial and lateral boundaries, alternately stands to the right and to the left side of the middle line of the patient. The *lateral upper limit of resonance* crosses the margin of the M. trapezius about 5 cm. medialward from the acromion, and thence runs (both in front, and on the back) downward (and slightly lateralward) towards the axilla. The widths of the zone of resonance at the margin of the M. trapezius amounts normally to from 6-7 cm.

These areas of Krönig do not, of course, correspond to the anatomical projection of the lung apices, but represent only the "areas of resonance," due to the apices. Goldscheider's method, on the other hand (threshold-

value percussion, with sagittally directed percussion stroke) gives, he asserts, almost exactly the anatomical projection of the lung apices on the front of the chest. Normally, the upper margin of the lung reaches a point, above the clavicle, corresponding to the position of the tubercle on the first rib, which can be felt, on palpation, between the heads of the sternocleidomastoid muscle. Goldscheider, accordingly, determines first the position of the upper margin between the two heads of the muscle, then maps out the medial boundary, and subsequently by percussion of the first rib itself delimits the subapical parts. Though his method seems to yield accurate results in his hands, it is difficult to apply in practice. Considerable skill is required, and the room must be absolutely quiet. Moreover, the older methods, though they yield percussion areas that do not correspond to anatomical projections, permit one to recognize pathological changes in a satisfactory way, and, as Gerhardt emphasizes, through them, we are able to percuss the apical region from three sides, so that anomalies are less likely to be overlooked.

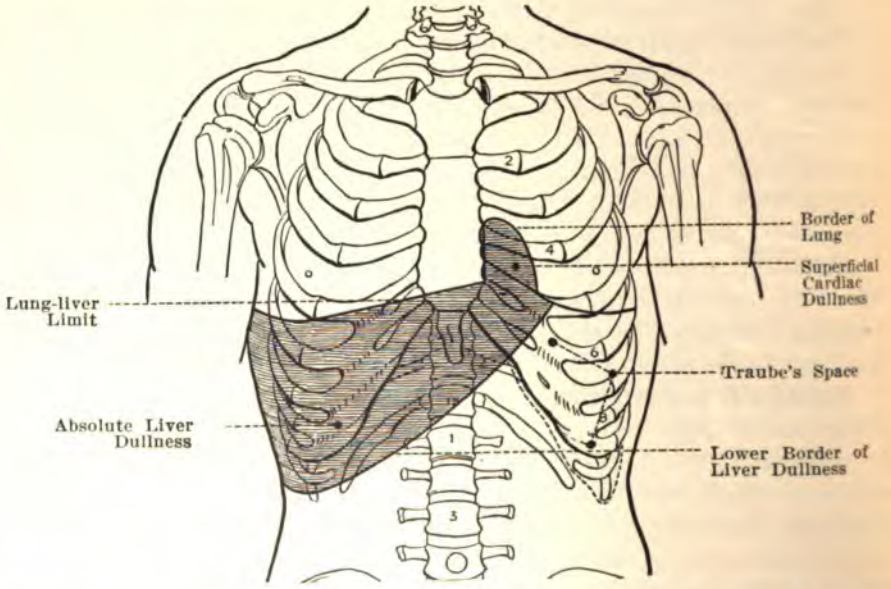

Fig. 155.—Normal Percussion Boundaries of the Lungs, the Liver, the Spleen, and Traube's Space on the Anterior Surface of the Body.

The Lower Limits of the Pulmonary Resonance on Percussion.—These can be easily determined by gentle percussion according to the methods described above, except at the junction of the left-lung resonance and the stomach tympany (lateral from the left mammillary line).

The limits should be determined during quiet breathing. The normal limits are as follows:

Right Side.—(1) In the *lateral sternal line,* the lower margin of the 5th-6th rib;

(2) In the *mammillary line,* between the lower margin of the 6th and the upper margin of the 7th rib;

(3) In the *axillary line,* the lower margin of the 7th or the upper margin of the 8th rib;

(4) In the *scapular line,* the 9th or 10th rib;

(5) Near the *vertebral column,* behind, the level of the spine of the 11th thoracic vertebra.

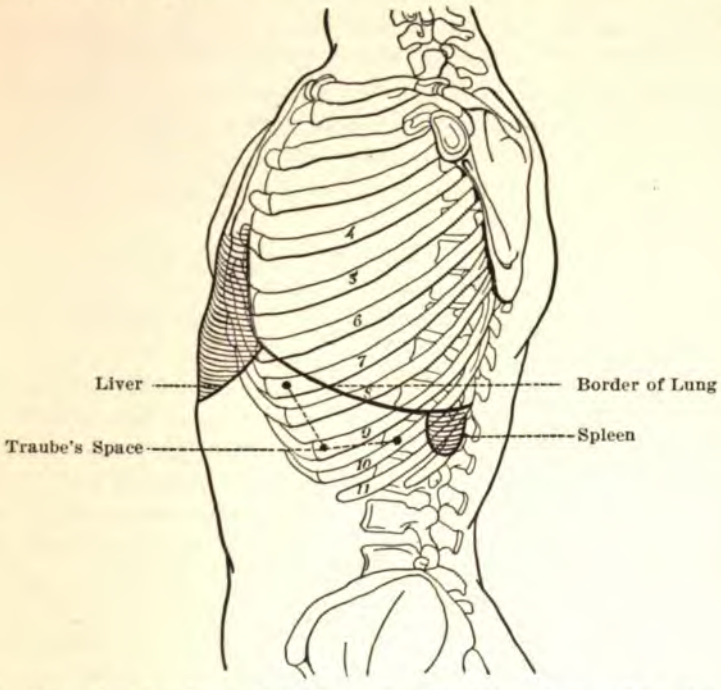

Fig. 156.—Percussion Boundaries of the Lung, the Liver, the Spleen, and Traube's Space on the Left Side.

Left Side.—The lower margin of the lung, beginning at the *sternum,* extends lateralward, behind the 4th rib, as far as the *parasternal line* (the lingula being too thin to yield resonance), and then behind the 6th rib; curving along the left margin of the superficial cardiac dullness, it turns, at the 6th rib, horizontally backward; in the *mammillary line,* it is at the lower margin of the 6th rib; in the *axillary line,* it reaches the level of the 7th-8th rib; in the *scapular line,* that of the 9th-10th rib; near the vertebral column, it is opposite the spine of the 11th thoracic vertebra.

This lower limit of the pulmonary resonance varies (1) with the phases of respiration, and (2) with the position of the patient. On forced inspiration, the boundaries may descend 2-3 cm. below the level found in quiet

breathing. In the dorsal decubitus, the lower margin is 1-2 cm. below its position in the sitting posture; in the lateral decubitus, that of the upper lung may descend 3-4 cm. lower.

The medial margins of the lung, in front, are outlined when the superficial cardiac dullness is determined (*q. v.*).

Abnormal Position of the Boundaries of the Lungs.—The determination of the lung limits may, in pathological states, show (1) a general expansion, (2) a displacement only of the lower boundaries, (3) a general contraction, or (4) a displacement either of the lower, or of the upper limit.

General expansion of the lung limits is met with in chronic emphysema and in the temporary inflation of the lungs due to tracheal or laryngeal stenosis, diffuse bronchitis and bronchiolitis, or asthma. The lower limit may be lower than normal from compensatory emphysema of the lower part of the lung (a) when the upper part is diseased (*e. g.*, in apical tuberculosis), or (b) when the lung is diseased on the opposite side of the body.

General contraction of the lung limits is met with when the total amount of air-containing tissue in the lungs is diminished from any cause (cirrhosis of the lung, prevention of entrance of air into the lung, compression of the lung).

The *lower limit of a lung may be higher* than normal (a) when the diaphragm is high (abdominal distention), (b) in retraction of a lung (from cirrhosis, or from tuberculosis), or (c) when parts of the lung are deprived of air (bronchostenosis, etc.). A very common cause for displacement of the lower limit of pulmonary resonance upward is the accumulation of fluid in the pleural cavities. When the pleura is non-adherent, the fluid tends to accumulate chiefly in the lateral parts; the line of the dullness does not, as a rule, run horizontally, but in a curve, the highest point of which lies approximately in the posterior axillary line, descending rather abruptly in front, and more gradually behind (Ellis' curve, S-shaped line of Gardner, parabolic dullness-curve of Damoiseau).

Retraction of the upper limit is most often due to pulmonary tuberculosis. The retraction of the apex is usually first demonstrable at the upper medial margin in front, and by Krönig's method can be demonstrated also at the upper medial margin behind.

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(*d*) *Comparative Percussion of the Lungs*

It should be kept in mind that, even in health, the pulmonary resonance on percussion varies somewhat over different areas of the thorax corresponding (1) to the variable thickness of the soft parts, and (2) to the variable volume of lung beneath. In some places, the sound is louder (clearer), and fuller (longer), than in others. By repeated percussion of the healthy chests of different persons, one gradually fixes in his mind memories of the normal sounds heard, and of the normal resistance felt, on percussion over the lungs, and one learns gradually to estimate how much muffling, or dulling, of the sound may be due to varying degrees of obesity and to different degrees of muscular, and of mammary, development. The sound produced by percussion over the bones of the thorax (ribs, sternum, clavicles, scapular spines) is somewhat duller, shorter, and higher pitched than in the intercostal spaces. The percussion sound is nearly always somewhat clearer in front and at the sides than behind. In fat people, especially, the resonance on percussion over the back suffers markedly.

It is always well to compare the percussion sounds yielded by symmetrical parts on the two sides of the chest (*comparative percussion*), beginning with percussion of the supraclavicular fossae above and passing downward on the two sides over the several intercostal spaces, making sure to percuss always with the same force and to direct the stroke in the same way.

The breathing should be shallow during the examination, since, on feeble percussion, the sound produced is duller, shorter, and higher in pitch during inspiration, while, on strong percussion, it is lower in pitch during inspiration.

The loudest sounds are normally met with between the third and the fifth rib in front. The sound is a little feebler and shorter between the second and the fourth ribs on the left side than on the right; from the fourth rib downward on the right, the sound begins to be shorter, owing to the relative liver dullness.

In comparative percussion, too, the influence of (a) the cardiac dull-

ness, (b) the tympanitic space of Traube (4th-6th rib on) due to the stomach in the lower part of the left front, and (c) the slight asymmetry of the two apices of the lung, on the pulmonary resonance, must be kept in mind. Further, slight asymmetries of the two sides of the thoracic wall are important in comparative percussion; even a slight grade of scoliosis may affect the sounds.

Behind, the percussion sounds are less loud, and of shorter duration, over the shoulder blades; beneath the angle of the scapula, they become louder and fuller, rather more so on the left than on the right on account of the relative liver dullness.

In pathological conditions, changes in the normal intensity, duration, and pitch are recognizable. (See below.)

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i. Dullness and Flatness on Percussion

The percussion sound may be dull, where it is normally loud, in all conditions in which the air content of the portion of the lung percussed is less than normal.

This may be due (1) to infiltration of the lung; (2) to collapse, or atelectasis, either from external pressure, or from absorption of the air after bronchial occlusion; or (3) to the presence of fluid, or of abnormal tissue, between the lung and the thoracic wall.

In order that airless lung shall be recognizable on percussion, the area deprived of air must be at least as large as the pleximeter used, and must extend 2 cm. deep.

Infiltration of the lung occurs in pneumonia (croupous and catarrhal), tuberculosis, hemorrhagic infarction, abscess, and neoplasm; *atelectasis* of the lung may be due to compression (pleuritic or pericardial exudates, or neoplasms), or to absorption of the air from the alveoli after the bronchi have been plugged (bronchial stenosis).

When the lung is separated from the chest wall by fluid (pleural effusions, empyema, hydrothorax), there must be at least 400 c.c. (in the adult) to yield dullness on percussion. Pleuritic thickening, and neoplasms separating the lung from the chest wall, can also cause dullness.

The boundaries of the dullness, due to the fluid in exudative pleuritis, change as a rule but little, if at all, with change of position of the patient (encapsulation by adhesions); in hydrothorax, which is usually bilateral though it may be unequal on the two sides, the level of the fluid changes with change of position, but only slowly after 15-30 minutes. An immediate change of the dullness (in the case of fluid in the pleural cavity) with change of position, indicates the simultaneous presence of air and fluid (pyo- and seropneumothorax); in such cases, the patient, on sitting or on standing, may present dullness in both lower fronts, while, when lying on his back, the fluid sinks backward at once and the percussion sound becomes loud in front where it was previously dull.

Pathological Fullness or Emptiness of the Sound.—In pulmonary emphysema, and in pneumothorax, the percussion sound is abnormally full (rich in tones of low pitch). A pathologically empty sound is met with in most cases where the note is abnormally dull, though emptiness (shortness) and dullness, as has already been pointed out, are not synonymous terms.

ii. Pathological Tympanitic Sounds on Percussion Over the Lungs

Aside from the tympany in Traube's space (lower left front), due to gas in the stomach, any tympanitic sound elicited on percussion over an area corresponding to any portion of either of the two lungs is abnormal. Thus, tympany on percussion may be met with (1) in infiltrations of the lung; (2) in relaxation of the lung tissue; (3) in conditions in which air and fluid are present, at the same time, in the alveoli; (4) over large, smooth-walled, air-containing cavities in the lung tissue; and (5) sometimes in pneumothorax.

Tympany Over Infiltrated Lung.—The tympanitic sound heard over infiltrated areas of the lung tissue is due to the better conduction between the thoracic wall and the normal air-containing cavities of the chest (bronchi). The note is simultaneously dull and tympanitic (*e. g.*, in pneumonias, and in compressions of the lung and other atelectases). This tympanitic bronchial sound is more often elicitable over the upper lobes (owing to the thinner chest wall there) than over the lower; the pitch is, in such cases, slightly altered when the patient opens and closes his mouth, but not on change of position of his body.

Tympany Over Ralaxed Lung.—Relaxed lung tissue yielding a tympanitic note may exist (1) in the neighborhood of extensive infiltrations, or of pleuritic and pericardial exudates (Skodaic resonance), (2) owing to compression of the lung from enlargement of the heart or liver, or from tumor growths, or (3) when the bronchi are occluded. The tympanitic note

elicited in such circumstances does not change in pitch on opening and closing the mouth. A tympanitic note over one upper lobe may arouse suspicion, early in the physical examination, of the existence of a pneumonia, or of other cause of relaxation of lung tissue, in the lower lobe on the same side. If, at autopsy, a relaxed lung be percussed on removal from the body, it will yield a tympanitic sound; if it be subsequently blown up, the tympany will diminish.

Tympany Over Lung Containing Air and Fluid in the Alveoli.—Air and fluid in the pulmonary alveoli yielding a tympanitic note are met with in the first and third stages of croupous pneumonia, in catarrhal pneumonia, in pulmonary edema, and, occasionally, in hemorrhagic infarcts.

Tympany Over Certain Cavities.—A tympanitic percussion sound can be brought out over cavities (tuberculous, gangrenous, bronchiectatic), when they are as large as a walnut, or larger, when their walls are smooth and not too tense, and when they are close to the surface of the lung, or are situated in the interior of infiltrated tissue. (For the change of pitch over such cavities, see below.)

Tympany Over a Valvular Pneumothorax.—Over a pneumothorax, especially of the valvular variety in which the air may be under great tension, a tympanitic percussion sound may sometimes be elicited. In most cases of pneumothorax, however, the percussion sound is not tympanitis, but is abnormally loud, and of low pitch.

iii. Variations in the Pitch of Tympanitic Percussion Sounds

In listening to tympanitic sounds elicited on percussion, we pay attention, especially, to the dominant tone. The pitch of this dominant tone has been found to be variable under certain conditions immediately to be described.

1. **Wintrich's Change in Pitch.**—In this type, the tympanitic percussion sound becomes higher in pitch on opening the mouth, and lower on closing it. It can be imitated by percussing on the cheek while the mouth is opened and shut. This variation in pitch is met with (1) over those cavities in the lungs that communicate freely with a bronchus; it is also sometimes observed (2) in the form of pneumothorax in which there is open communication with a bronchus, and (3) over a pneumonia, or above a large pleuritic exudate (owing to percussion vibration of the air in the bronchi through the infiltrated or relaxed tissue). If Wintrich's variation in pitch be present in one position and absent in another, it is probable that, in the position in which it is absent, the conducting bronchus has been occluded by fluid ("interrupted Wintrich's change of pitch").

2. **Friedreich's Change in Pitch.**—This is less important; by it is meant the change in pitch of a tympanitic sound over a cavity during respiration; the sound becomes higher in pitch on inspiration, and lower in pitch on expiration.

3. **Gerhardt's Change in Pitch.**—This is met with over oval cavities partially filled with fluid. If the long axis of the cavity be in the sagittal direction, the pitch of the tympanitic percussion sound is higher on sitting than on lying; if the long axis of the cavity be in the anteroposterior direction, the pitch is lower on sitting than on lying; in other words, a shortening of the long diameter of the cavity heightens the pitch. This is interesting, but practically unimportant.

4. **Biermer's Change in Pitch.**—By this is meant the change in pitch that is met with sometimes over seropneumothorax; the pitch of the percussion sound is lower on sitting than on lying owing to the fact that, in the sitting position, the pressure of the fluid causes descent of the diaphragm and increases the area of the resounding space.

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iv. Metallic Sounds Over the Lungs

The characters of these metallic sounds have been described above.

A *metallic ring* is heard on percussion over the thorax: (1) in pneumothorax; and (2) over large, smooth-walled cavities (diameter of 4 cm. and more). The "coin sound" is a metallic ring.

The *cracked-pot sound* may be heard on percussion (1) over superficial cavities that communicate, through a narrow opening, with the bronchi, and (2) sometimes over relaxed and infiltrated lung tissue. The cracked-pot sound is best elicited when the patient holds his mouth open; the examiner's ear or the bell of the stethoscope should be held close to the open mouth.

8. Auscultation of the Lungs

In health, and in disease, various sounds arise within the body; by listening to these (*auscultation*), we can draw certain inferences regarding the structure, or the conditions, of the organs in which they arise.

On auscultation of the lungs we listen to (1) the voice sounds audible over the thorax; and (2) the sounds that accompany inspiration and expiration.

We listen either (1) with the naked ear separated from the chest wall by a thin towel (*immediate ascultation*), or (2) with the aid of a stethoscope (*mediate auscultation*).

The voice sounds are better heard with the naked ear than with the aid of a stethoscope, but the breath sounds, and, especially, some of the modifications that these undergo in disease, as well as some of the sounds that accompany them, are better recognized and localized by the use of the stethoscope.

On examining the front of the chest, the stethoscope is better than the naked ear, for obvious reasons. On the other hand, the ear applied directly to the chest is often most useful in examining the back.

In patients that are very ill, lying on their backs in bed, and especially when they are very heavy, a Bowles stethoscope may be found convenient, since it permits of a more extensive examination with less change of position than other forms in use. For ordinary work, the Ford stethoscope is a good model. In some countries, the monaural wooden stethoscope is still highly prized; in North America, the binaural stethoscope is everywhere in use and a monaural instrument is rarely employed.

(*a*) *Auscultation of the Voice Sounds Over the Thorax*

In practice, one begins the auscultation of the chest by listening to the breath sounds, and then afterwards listens to the voice sounds; but in a systematic consideration of thoracic auscultation it is better to approach the subject by way of the voice sounds, since their origin is much better understood.

In studying the voice sounds we have to consider, first, their origin, and next the changes that they undergo on conduction through the air passages and the lungs to the chest wall.

i. Origin of the Voice Sounds

Here two processes play important parts: (1) the production of fundamental tones in the larynx, where the vocal cords of the glottis act like a reed instrument; and (2) the process of articulation, in which the different tones produced in the larynx are modified by changes in shape of the mouth cavity, and adjacent cavities, the larynx itself being wholly unable to articulate. The mouth cavity, in association with the laryngeal and nasal cavities, constitutes a resonating chamber. As such, it intensifies that particular tone or overtone of the sound produced in the larynx the wave-length of which corresponds in resonance to the dimensions of the cavity. Variations in the shape of the cavity will modify its function as a resonating chamber in that it will vibrate in unison with notes of different wave-length or pitch. Thus, through changes in the resonating chamber, different overtones may be intensified or weakened and corresponding changes in the voice sounds produced. In whispering, there is articulation of the breath sounds only, the glottis being passive and giving rise to no loud tones.

ii. Changes in the Voice Sounds After Their Formation

These sound waves of the glottis, articulated by the mouth, pass backward through the narrow glottis into the trachea, and thence, through the bronchi, to the deeper portions of the lung. Owing to the fact that the current of air is in the opposite direction and that the articulated tones are compelled to pass through the narrow opening of the glottis, the sound waves that pass down the trachea are, on the way, somewhat altered. Beyond the bifurcation of the trachea, the sound waves spread through the diverging ramifications of the bronchi; the sounds become weak and muffled, probably owing to the diminution in the rigidity of the tubes and to the increased conduction of the vibrations away from the air columns by the tissues, owing to the increased surface exposed to the sound waves. The lung tissue in its natural distended state is such a bad conductor that the sounds in the large bronchial tubes are not audible over the thoracic wall.

iii. Voice Sounds Audible Over the Thorax in Healthy Persons

Now when one listens to the voice sounds over the healthy lung of a person pronouncing the number "99" in a voice of low pitch, the sounds audible are nearly everywhere weak and muffled (*normal voice sounds*), instead of being loud and clear like those audible over the larynx. In women and children, indeed, voice sounds may not be audible at all over a large part of the chest. In many healthy persons, however, quite loud and relatively clear voice sounds are audible in the back over the spinous processes of the upper thoracic vertebrae (opposite the trachea and the bifurcation of the bronchi). When loud, clear voice sounds are audible directly over the bronchi of the healthy chest, the condition is known as bronchophony, the term bronchophony including such sounds audible in health and all degrees of clearness greater than this in disease when the voice sounds audible over the thorax may become almost as loud and clear as those audible over the larynx (*pathological bronchophony*). It has been the practice of many clinicians to use the term *vocal resonance* when describing the voice sounds audible over the thorax; this is unfortunate, for resonance has very little to do with the origin of the sounds, either in health or in disease, and the term vocal resonance should, therefore, in my opinion, be discarded.

iv. Coughing Sounds and Crying Sounds

What applies to the voice applies also to the cough and the cry. One has to depend upon these sounds rather than upon the voice sounds on making the physical examination of the chest in young children.

v. Abnormalities of the Voice Sounds Audible Over the Thorax

The voice sounds audible over the chest may be either feebler and less distinct, or louder and more distinct, than normal. We pay attention, however, to clearness or distinctness rather than to loudness of the sounds, since distinctness and loudness are often opposed to one another, and it is the former that is important for diagnosis rather than the latter.

Diminished clearness or distinctness of the voice sounds is of little value for clinical diagnosis. Since, normally, the sounds are muffled and, in some persons, wholly inaudible, unless one note that the sounds have become less clear where formerly they were more distinctly heard, but little attention need be paid to the sign. Occlusion of the bronchi is the most common cause of such diminution of distinctness; other causes include (1) pleural effusion, (2) thickened pleura, and (3) large masses of fat or muscle between the skin and the lungs.

Increased clearness or distinctness of the voice sounds **(pathological bronchophony)** is the term applied when sounds as clear as, or clearer than, those heard over the upper thoracic spine in health are met with in any other part of the chest, since nowhere else are they normally present. The phenomenon is due either to increased conducting, or to increased reflecting power, of the lung tissue. The conducting power of the spongy structure of the lung is increased by any change that makes the lung structure more homogeneous. Thus the lung becomes more homogeneous (1) when it becomes more solid (infiltration, collapse, neoplasm, compression), or (2) when it contains more air (cavities from bronchiectasis, tuberculosis, or gangrene; marked emphysema). When cavities exist, there is increased reflection of the sound waves in addition to the improved conduction. In normal alveolar tissue, reflection of sound practically ceases, but, in cavities, reflection of the waves may be as great as in normal bronchi. In large smooth-walled cavities, the reflection may be so great as to yield a highly reverberating character to the voice sounds (*cavernous voice sounds*).

Whispered bronchophony is sometimes clearer than that of the voice. The terms *pectoriloquy*, and *whispered pectoriloquy*, are sometimes applied when the sounds are very clear, apparently close to the ear, and exactly circumscribed. It is maintained by Baccelli that clear pleural exudates conduct the whispered voice (*voce afona*) better than exudates rich in cells (*e. g.*, in empyema). Too much stress should not, however, be laid upon "Baccelli's sign."

A special kind of bronchophony known as **egophony** is sometimes heard above the level of the fluid in large pleural effusions that cause partial compression and narrowing of the bronchi. The voice sounds have a more nasal quality than is usual; there is an echoing quality to the sound and it is rhythmically intensified and interrupted. The term egophony

was applied by Laennec to indicate the similarity of the sound to that of the bleating of a goat; he also compared the sound to the voice of Punch.

Over large cavities containing air, and especially over a pneumothorax, the voice sounds may have an amphoric, metallic, ringing quality (*amphorophony*).

Auscultation of the voice sounds yields information comparable in large part to that afforded by palpation of the vocal fremitus; when the voice is not strong enough or deep enough to yield a palpable fremitus, auscultation of the sounds may give information not otherwise obtainable.

(*b*) *Auscultation of the Breath Sounds Over the Thorax*

During respiration, the breath sounds (inspiratory and expiratory) are audible over the lungs. When one listens over the larger air tubes, a certain quality is present that is absent when one listens over the alveolar masses of the lung. The former type is called *bronchial breathing*, and the latter *vesicular breathing*.

In diseased states, owing to the secretion of mucus, to swelling of the bronchial mucous membrane, or to fibrinous exudation upon the surfaces of the pleurae, certain accessory or *adventitious sounds* arise (râles, crepitation, friction sounds), distinguishable from the actual breath sounds.

i. Vesicular Breathing

On inspiration, a soft blowing murmur is audible over the healthy lung and, on expiration, either no sound at all, or a feeble blowing or aspirating sound can be heard; these sounds are those of normal vesicular breathing. The inspiratory sound can be imitated by placing the mouth and lips in the position of articulating the letter *f* and drawing in air; the expiratory sound can be simulated by driving out air with the lips in the same position.

Origin of Vesicular Breathing.—There has been much dispute as to the origin of the normal inspiratory and expiratory breath sounds. Many have been attracted by the view that the glottis is the only source of the breath sounds. The passage of the inspired and of the expired air, through the narrow glottis, into wider spaces above and below it gives rise to "fluid veins"; the sounds thus arising, modified by resonance in the pharynx above and in the trachea below, are conducted down the air tubes, just as the voice sounds are carried (*vide supra*). Owing to the bad conducting qualities of alveolar tissue, the glottidean sound is converted into the inspiratory and the expiratory, vesicular breathing, while, over the larger bronchi, the glottidean sound approaches its primary intensity and quality (bronchial breathing). More recent study and criticism indicate, however, that, though the above explanation probably holds for the expiratory part of vesicular breathing, it is inadequate fully to explain the origin of the inspiratory sound. The tendency at present is to accept the view of Gerhardt, who assumes that, during inspiration, there are actual vibrations of the alveolar lung tissue, which is made tense by the entrance of the air. Gerhardt grants that the very

feeble, scarcely audible, sound of expiration is a bronchial sound weakened by the alveolar tissue.

Variations in the Breath Sounds in the Normal Chest.—The inspiratory and expiratory breath sounds just described are audible over the whole chest, though the intensity varies (1) with the depth of the respirations, and (2) with the condition of the lung over which one listens.

The breath sounds are, normally, loudest just beneath the clavicles, where the thoracic walls are thin and where the pulmonary tissue is best ventilated; over the apices, the sounds are feebler. When, on auscultation over a definite area of the chest wall, one hears pure vesicular breathing, it is fair to conclude that air-containing tissue lies beneath this area and participates in respiration.

Modifications of Vesicular Breathing in Disease.—Clinically, one has to observe whether the vesicular breathing is of normal intensity, is abnormally loud (accentuated), or is abnormally weak (enfeebled).

Loud, or accentuated, vesicular breathing, or roughened breathing, is met with normally in children, and is hence often spoken of as PUERILE BREATHING, the air on inspiration entering the very elastic child's lung with greater force; this puerile breathing is often audible during adolescence, for a longer period in girls than in boys.

When such roughened breathing is heard over a part of the lung in the adult, it may indicate obstruction to the entrance of air into some part of the lung other than that where the roughened breathing is heard; thus it is often audible in the neighborhood of infiltrated areas, especially at the apex, in incipient pulmonary tuberculosis, and in healthy lung close to a consolidating area, at the beginning of pneumonia.

Sometimes there is PROLONGATION OF THE EXPIRATORY SOUND of vesicular breathing so that this becomes as long as, or even longer than, the inspiratory sound. This change is met with sometimes, normally, in the supraspinous fossae. The expiratory sound may also, normally, be a little longer over the right apex than over the left. Elsewhere, a prolongation of the expiratory part of the vesicular breath sounds usually indicates an expiratory dyspnea (emphysema, asthma, bronchitis), if the distribution be general; or a beginning infiltration, if it be local.

If the inspiratory sound, instead of being continuous, be interrupted so as to consist of two or more parts, the inspiration assumes a jerking, or saccadate character (COG-WHEEL BREATHING). Assuming that the muscular contractions are smoothly and evenly made during inspiration, such jerking breathing occurs when local, quickly yielding, obstructions to the entrance of the air current into the alveoli are temporarily overcome. The sign has been looked upon as of importance for the diagnosis of beginning apical tuberculosis. Too much stress should not, however, be laid upon it, since it is often met with in persons of feeble musculature, in nervous

people, and in children after crying. This sign has also been observed in insufficiency of the pulmonary valves of the heart; here it seems to be due to the fact that the sudden regurgitation of blood into the right ventricle during diastole gives rise to a phenomenon in the pulmonary capillaries comparable with the capillary pulse that appears in the general circulation in aortic insufficiency.

Enfeeblement, or SUPPRESSION OF VESICULAR BREATHING, occurs whenever the inspiratory expansion of the lungs is interfered with. When bilateral, it may be due to tracheal or laryngeal obstruction, or to emphysema. More often, it is unilateral, in which case it may be due to: (1) obstruction of a large bronchus (fibrinous bronchitis, aortic aneurism, fibrosis); (2) to separation of the lung from the chest wall in pleurisy, hydrothorax or pneumothorax; the vesicular breath sounds may be entirely absent over large pleuritic effusions; or (3) to the prevention of deep inspiration from pain, especially from the pain due to pleuritic involvement over the affected lobe at the beginning of an infiltration in lobar pneumonia.

ii. Bronchial Breathing

The peculiar character of *bronchial breathing* is best learned by listening to it. It is difficult adequately to describe it. It has an aspirate character and may be artificially imitated by making the lips and mouth assume the attitude used in pronouncing *h* or *ch* and then forcibly breathing in and out.

Bronchial Breathing Audible Over the Normal Thorax.—Such bronchial breathing is audible even in healthy persons over the spinous process of the 7th cervical vertebra, corresponding to the position of the bifurcation of the trachea; it can also be heard, close to the spine, in the intercostal spaces down as far as the spinous process of the 5th thoracic vertebra, since, here, the larger bronchi lie near the surface. Still louder and more intense sounds are audible, normally, over the trachea (*tracheal breathing*), and over the larynx (*laryngeal breathing*).

The sounds arise, chiefly, in the glottis; they are due to liquid veins, which arise, below and above this narrow slit, on inspiration and on expiration. The air in the trachea and bronchi is set into vibration so that a clanglike sound is produced by the air tubes, which, like organ pipes, are attuned to a certain fundamental tone.

Thus, the inspiratory sound arises when air passes from the choanae into the nasopharynx and from the glottis into the larger laryngeal cavity and into the trachea; and the expiratory sound arises when the air passes through the glottis into the supraglottidean portion of the larynx. The loudness of bronchial breathing is not important. It is the special quality of the sound—the aspirating, hollow or reverberating character—that is

wide-mouthed bottle or jar. Metallic breathing, and amphoric echo or hum, when heard, indicate the presence either of a large cavity, or of a pneumothorax, being observable in the latter especially when there is a wide fistula connecting the pneumothorax with a large bronchus.

iii. Mixed Breathing, Bronchovesicular Breathing, and Indefinite Respiration

In certain areas one sometimes hears bronchial breathing and vesicular breathing simultaneously, sometimes one component, sometimes the other, being dominant. This is often referred to as mixed breathing, or **bronchovesicular breathing.** It arises where the conditions for the occurrence of bronchial breathing and of vesicular breathing exist alongside one another and where, accordingly, neither of these types of breathing is audible in a pure state. Thus it may be met with in beginning, or in incomplete, infiltration of the lung tissue, especially where small foci of solidification alternate with areas of air-containing tissue (*e. g.*, in tuberculosis, in diffuse infiltration, and in bronchopneumonic foci).

The so-called **indefinite breathing** (*unbestimmtes Atmen* of the Germans) is usually such mixed breathing, though, in some instances, it is enfeebled vesicular breathing, or weak bronchial breathing. Thus, over pleuritic exudates or when loud râles are present, the respiratory murmur may be so feeble that one cannot distinctly recognize its character. In slowly-developing infiltrations of the lung, the first change noticeable in the breath sounds is, often, a lengthening and roughening (or sharpening) of the expiration following normal vesicular inspiration. Later, the inspirium becomes indefinite while the expirium assumes a bronchial character; finally, when the area is wholly deprived of air, the inspiratory sound also becomes bronchial.

In both bronchial breathing and mixed breathing one should note whether the sound is loud or feeble. Feeble bronchial breathing is often heard behind a pleuritic exudate and may be due either to pneumonic infiltration, or to simple collapse from compression by the exudate.

By **metamorphosing breathing** is meant the form in which the breath sound audible during inspiration suddenly changes in character. Usually, it begins with a sharp hissing sound and then changes to a softer bronchial breathing. It was described by Skoda as a "veiled puff" and is probably identical with the *souffle voilé* of Laennec. It is believed that it is due to the sudden removal, at a certain stage of inspiration, of some obstruction to the passage of air through a bronchus that communicates with a cavity.

iv. Accessory or Adventitious Respiratory Sounds Audible in Disease

In addition to the natural breath sounds (vesicular and bronchial breathing) and the changes these undergo in disease, certain sounds arising

inside and outside the lung, wholly additional to those described above, must now be considered. Of such adventitious respiratory sounds, we distinguish two great groups, (1) râles, or crackles; and (2) friction sounds.

Râles; Crackles; Rhonchi

These are sounds that arise during respiration from movements of abnormal contents of the air passages by the air breathed. They may arise (1) from the presence of fluid (mucus, serum, blood, etc.) in bronchi and in cavities, leading to the formation of air bubbles that break; (2) from the movement of different masses of mucus or secretion; (3) from the sudden separation of sticky mucous membranes; and (4) from the passage of air through abnormal local narrowings.

These sounds may, in intensity, be loud or feeble, in frequency, numerous or few; they are most often inspiratory in time, though they may occasionally be audible during expiration (rhonchi particularly). On testing for the presence of râles, one listens while the patient is asked to take a deep breath or to cough. It is important to notice whether the râles disappear or are modified on coughing. We divide râles into two great groups: (1) dry râles, and (2) moist râles.

Dry Râles, or Rhonchi.—These are rather long, whistling or snoring sounds that die away slowly. They are due to the vibration of tough mucus attached to the walls of the bronchi, or to the passage of the air through lumina narrowed by spasm of the bronchioles or by swelling of their mucous membrane. They are often accompanied by palpable vibration of the chest wall. The sounds, when low pitched, have a snoring character (*sonorous rhonchi*); when high pitched, they are more whistling or piping in character (*sibilant rhonchi*). The sonorous rhonchi probably arise in the larger tubes, the sibilant in the smaller tubes.

Moist Râles.—These sounds arise when fluid is present in the air passages. They are crackling or bubbling sounds that resemble the noises produced in bubbling fluids, and they may be very well imitated by blowing into a glass of water through straws of different sizes. In contrast with the more continuous, chiefly expiratory, sounds described above as sibilant and sonorous rhonchi, these moist râles are interrupted, bubbling or crackling sounds, heard chiefly during inspiration.

The moist râles are sometimes classified according to the apparent size of the bubbles or crackles, the larger bubbles being known as *gurgling râles*, those next in size as *medium sized bubbling râles* or crackles, and those of smaller size as *fine crackles*, or as *subcrepitant* and *crepitant râles*. The sound of the so-called crepitant râle can be very well imitated by rubbing a lock of the hair between the fingers close to the ear, or by separating the moistened surfaces of the thumb and forefinger when in

contact beside the ear. These sounds are not unlike the sounds of salt crackling in a fire, or of the sizzling of soda water. Such crepitation consists of numerous small crackling sounds of even size, heard chiefly, and usually exclusively, during inspiration. It is met with in pneumonia in the stage of engorgement (*crepitatio indux*) and also in the stage of resolution (*crepitatio redux*). It may also be heard in pulmonary edema, and in atelectasis where some of the collapsed alveolar walls or walls of minute bronchioles are torn apart by entering air currents. In feeble patients, and during convalescence from severe disease, one often hears, on examination, such crepitation in the lower and posterior parts of the lung during the first deep inspirations taken.

The crepitant râle, no matter in what condition it is met with, is believed to be due to the opening up of collapsed air sacs or minute bronchioles; occasionally, it may be a very fine mucous râle. It is distinguishable from other moist râles (1) chiefly, by the short duration, or small size, of each of the successive crepitations; and (2) by the large number of crepitations attending each inspiration.

Small mucous râles approaching the crepitant râle in duration and in size are sometimes called *subcrepitant râles.*

Ringing (or Consonating) and Non-ringing (or Non-consonating) Râles.—Râles that seem to be close to the ear and to be attended by a certain clang (not, however, an outspoken metallic sound) that does not accompany ordinary râles are said to be "ringing" or "consonating" râles. These are usually rather large, bubbling sounds, arising in a cavity or in a larger bronchus, and well propagated to the surface through infiltrated lung tissue; the higher tones are strengthened through resonance in the bronchi. When air-containing tissue lies between the cavities or bronchi in which the râles arise and the wall of the thorax, the râles are not ringing or consonating. This ringing character of a râle is therefore of considerable diagnostic importance in infiltrations of the lung. Consonating râles occur under the same conditions in general as does bronchial breathing; they sometimes help us out in diagnosis when the breath sounds are indefinite (*e. g.*, over small bronchopneumonic foci).

Gerhardt suggests that the difference in sound between consonating and non-consonating râles can be well imitated by blowing through a glass tube into water, contained, in the one case in a high glass or bottle, in the other in a flat saucer or soup-plate.

Metallic Ringing Râles.—These occur under conditions similar to those in which a metallic clang on percussion and metallic bronchial breathing (*q. v.*) occur. They have, accordingly, the same significance, indicating either cavities in the lung or a pneumothorax.

A special sound to be considered here is the so-called *metallic tinkling,* or *sound of the falling drop,* first alluded to by Thomas Willis. It was compared by Laennec to the sound produced in a metal or a porcelain cup,

when it is struck gently by a pin. It is a single sound, tolerably constant on coughing, a little less constant on speaking; with the breath sounds, it is usually heard intermittently, not accompanying each respiratory movement. The patient may sometimes hear it himself. It occurs most often in pyopneumothorax, or in large tuberculous cavities; and it appears to be due to a large drop falling upon the wall of the cavity or upon the surface of its fluid content, though, sometimes, it may be due to the bursting of a bubble. The relatively low pitched sound heard at first is followed by a high, harmonic or "metallic" echo; smooth walls and a resonating cavity are prerequisites to such a sound.

Cardiopneumatic murmurs, or cardiac râles, are referred to in the section dealing with Diseases of the Heart.

Pleural Friction Sounds

These arise during respiration from the rubbing together of the pleural surfaces, roughened by fibrinous, inflammatory exudates.

They arise most often between the costal pleura and the pulmonary pleura, but they may arise between the pulmonary pleura and the mediastinal pleura, or between the pulmonary and the diaphragmatic pleura. The sounds may be fine (soft, aspirative), or coarse (scratching, creaking); and they may be loud (intense), or feeble.

The softer, gentler friction sounds may sometimes be confused with vesicular breathing; the coarser, crackling friction sounds may occasionally be mistaken for râles. The pleural friction sounds can, however, generally be recognized as such, if one bear the following facts in mind: (1) they seem close to the ear; (2) they are intensified by pressure of the stethoscope; (3) they are often accompanied by a palpable friction fremitus; (4) they do not disappear, nor are they, as a rule, much modified, on coughing; and (5) they are usually accompanied by pain, whereas intrapulmonary sounds are not. Pleural friction sounds indicate the presence of a "dry" pleurisy in the region in which they are audible. In milary tuberculosis involving the pleura, soft friction sounds may be heard over large areas of one or of both lungs. Friction sounds sometimes become audible in tumors of the pleura, or when the pleura is merely abnormally dry (cholera).

Near the heart, pleural friction may be heard not only with the respiratory movements, but also synchronously with the heart's action owing to the rubbing of the pericardial pleura against the adjacent pulmonary pleura (*pleuropericardial friction*). The differential diagnosis between this extrapericardial friction and true pericardial friction is described under pericardial friction (*q. v.*).

Other Pleural Sounds

Besides (1) friction sounds, (2) the amphoric hum or metallic resonance (*q. v.*), and (3) metallic tinkling (*q. v.*), two other abnormal auscultatory phenomena referable to the pleura can sometimes be elicited by the physician on examination; namely, (4) the succussion splash, and (5) the coin sound.

Succussion Splash.—When the pleural cavity contains both liquid and air, and the patient is given a vigorous shaking while the physician listens to the chest, a splashing sound is heard (*Hippocratic succussion*). The patient may be able to hear it and to produce it at will himself. It is a metallic splash. Care should be taken not to confuse it with the splash produced in the stomach when the latter contains both fluid and gas.

Though this succussion splash is usually due to sero- or pyopneumothorax, it is occasionally heard in the absence of pneumothorax, when large cavities exist in the lung.

Coin Sound.—If one listens with the naked ear or with a stethoscope in front to the wall of the chest of a patient, while an assistant percusses at about the same level on the same side of the chest behind, using two coins as plexor and pleximeter, a clear ringing sound may be heard if a large cavity containing air exists in the lung, or if pneumothorax be present. This sound contrasts markedly with the sound audible under similar conditions over the healthy chest or on the opposite, relatively normal, side of the patient's chest. This coin sound, sometimes spoken of as the "bell sound" or "metallic ring," is in reality identical with the metallic ring of percussion (*q. v.*) as heard by the ear close to the chest or through the stethoscope.

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[For other references, see under Percussion.]

9. The Relation of Physical Signs to Conditions in the Lungs and Pleurae

On examining the chest by the physical methods above described, one should try, at first, merely to draw inferences regarding the air content of the underlying lungs and the physical state of the pleural cavities, and only subsequently to seek the pathogenetic explanation of these physical conditions of the lungs and pleurae. In the table on page 527 a general view of the relations between physical signs and underlying conditions is presented.

10. Examination of Sputum

(*a*) *Sources of Sputum*

The sputum expectorated on hawking or coughing consists of a mixture of secretions from the mucous membranes with pus, blood or other materials given off from the respiratory apparatus. The secretions come from the mucous membranes of the larynx, trachea and bronchi, pharynx and back of the nose (choanae). In addition to the above, the sputum contains saliva, secretions from the mucous membranes of the mouth, and sometimes food particles.

It is obviously important to distinguish, when possible, the sputum that comes from the lungs and deeper air passages from that originating in the mouth or nasopharynx. *Pulmonary sputum* should be collected, whenever practicable, by methods that guarantee its relative freedom from admixture with constituents from the mouth, nose and nasopharynx (See Sputum Cultures). It may be received in a sterile Petri dish, or in a wide-mouthed bottle, previously cleaned, boiled in water, and dried. *Mouth sputum* usually consists chiefly of saliva and is recognizable as an opaque, sticky fluid in which, on microscopic examination, swollen, flat, epithelial cells and leukocytes, singly or in groups, are visible. *Nasopharyngeal sputum* consists chiefly of mucus more gelatinous than that in the saliva and met with usually in the form of roundish balls or lumps the size of a pea or bean, which do not run together, or mix well

PHYSICAL SIGNS OVER THE LUNGS AND PLEURAE IN DIFFERENT CONDITIONS.

STATE OF LUNG OR PLEURA.	INSPECTION.	VOCAL FREMITUS ON PALPATION.	PERCUSSION SOUNDS.	AUSCULTATION.		
				Voice sounds.	*Breath sounds.*	*Accessory sounds.*
Air-containing lung.	Normal expansion.	Normal.	Loud, not tympanitic.	Normal.	Vesicular.	If râles present from fluid in bronchi, they are non-consonating.
Solidified lung.	Expansion diminished.	Increased.	Dull (not flat), and slightly tympanitic.	Pathological bronchophony.	Pathological bronchial breathing.	Consonating râles.
Large air-containing cavities, or pneumothorax.	Expansion diminished. In pneumothorax, side usually bulging.	In cavities, increased; in pneumothorax, diminished or abolished.	Tympanitic, or metallic.	Over cavities, bronchophony; over pneumothorax, enfeeblement.	Amphoric (may be diminished over pneumothorax).	Metallic consonating. (Coin sound over pneumothorax.)
Fluid in pleural cavity.	Immobility; widening, and, if purulent, often bulging of intercostal spaces.	Diminished or absent.	Flat.	Weakened (distant) or absent; above the level of the fluid, egophony.	Weakened (distant), or absent.	Absent (friction rub audible only in dry pleurisy).

with the rest of the sputum. This mucus from the nasopharynx may be transparent or purulent; it may be gray or black from admixture with coal dust, or it may contain tough, dry, wrinkled scabs, yellowish, brownish or greenish in color.

When the sputum is purulent it is often difficult to decide whether the pus has had its origin in the mouth and pharynx or whether it has come from lower down. An admixture with saliva, or a very putrid odor, is suggestive of a buccal or a pharyngeal origin, though very fetid sputum is expectorated also in putrid bronchitis, in bronchiectasis and in pulmonary gangrene.

Sputum of pulmonary origin, when scanty, may sometimes be increased by the administration of a few doses of potassium iodid or ammonium chlorid. In early pulmonary tuberculosis, especially in children, the tubercle bacilli may sometimes be found in sputum swallowed during the early morning hours; the sputum is obtained by washing out the stomach before breakfast (T. Hausmann).

In handling sputum precautions should be taken to avoid personal infection. The sputum should be kept in well-covered receptacles until disposed of. In hospitals the sputa and sputum cups should be sterilized after examination in an autoclave. If chemical sterilization is relied upon a 5-per-cent solution of carbolic acid will suffice if the quantity of sputum be small.

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(*b*) *Varieties of Sputum*

According to the principal constituent, four main varieties of sputum may be described: (1) mucous; (2) purulent; (3) serous; and (4) bloody.

Other forms of sputum are admixtures of these (*e. g.*, mucopurulent, muscohemorrhagic, etc.). One should always notice whether the different constituents of sputum are intimately mixed with one another to form a homogeneous fluid, or remain separated from one another as recognizably different parts.

Mucous Sputum.—When the sputum consists of pure mucus it is usually either from the choanae or from a beginning bronchitis. Sputum from the choanae (nasopharyngeal) is usually hawked up; bronchitic sputum is coughed up.

Purulent Sputum.—When not from the mouth or the pharynx, pure purulent sputum (free from mucus) is due to the rupture of an abscess of the lung, or of a neighboring organ (empyema, liver abscess), into the bronchi.

Mucopurulent Sputum.—Mucus and pus may be intimately mixed with each other in the sputum in diffuse bronchitis. In bronchoblenorrhea, the thin mucopurulent sputum often separates on standing into *three layers.* Similarly, three layers are met with in bronchiectatic sputum, in lung gangrene, and in fetid bronchitis. The *upper layer* is frothy and consists of lumps and balls; the *middle layer* consists of thin mucus and serum with a few shreds hanging down from the upper layer; while the *lower layer* contains a sediment of confluent pus and whitish particles.

In pulmonary tuberculosis, the sputum contains pus and mucus, usually not well mixed, the pus appearing as ball-shaped or coin-shaped masses surrounded by mucus (*nummular sputum*). If large cavities exist in a tuberculous lung, nearly homogeneous sputum may be expectorated.

Serous Sputum.—In pulmonary edema, an abundant thin but very frothy sputum, resembling beaten egg-white, is expectorated, or may run out of the mouth. It may be colorless, but it is sometimes tinged with pink (blood). This form of sputum is highly characteristic and of great importance for diagnosis.

Bloody Sputum.—Sometimes pure blood is expectorated (HEMOPTYSIS) in bronchiectasis, in pulmonary tuberculosis, in leaking aneurism, and, occasionally, in lung abscess or in lung tumor. In hemoptysis, the blood is coughed up; it can be distinguished from the blood that is vomited up from the stomach (*hematemesis*) (1) by its bright red color, (2) by the froth in it, and (3) by the fact that it is not mixed with food.

When blood is intimately mixed with mucus in the sputum, the color varies according to the relative quantities of these two constituents and the length of time the blood has remained in the air passages before it is expectorated. Thus, in pneumonia, the sputum may have a brick dust tint (*rusty sputum*), or, especially in alcoholic cases, it may be outspokenly hemorrhagic. Mucohemorrhagic sputum is also met with in hemorrhagic infarction of the lung and in neoplasm.

The so-called *prune-juice sputum* is a serohemorrhagic sputum. It is met with when a croupous pneumonia is complicated by edema of the lung. A peculiar mucohemorrhagic sputum of sticky consistency, resembling currant jelly, is seen in neoplasm and sometimes in lung syphilis.

Small streaks of bright blood in sputa otherwise of mucous character usually originate in the upper air passages (nose, pharynx, larynx) or in the mouth.

Blood-stained saliva is often brought to the physician by the hysterical and by simulants; it is usually a thin fluid, of stale odor and of brownish-red color.

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(c) Color of Sputum

Aside from the above-mentioned purulent sputa (yellow or yellowish-green) and hemorrhagic sputa (red, brown, or yellowish-red), sputum may assume different tints from the admixture of various coloring matters.

Black sputum is seen in coal- and iron-workers; *blue sputum* is occasionally seen in workers in dye-works; *green sputum* is met with in pneumonia with jaundice, sometimes in caseous pneumonia, and occasionally in pyocyaneus infections; *yellow sputum* may be due to hematoidin in lung abscesses, or to bile when liver abscesses break into the lung. In chronic passive congestion of the lung in cardiac disease, a *yellowish-red* tint may appear, owing to the large number of pigment-containing cells —"heart-failure cells"—in the sputum. *White sputum* resembling starch is sometimes seen in bakers and in millers; the starch granules can be demonstrated microscopically.

(d) Odor of the Sputum

Usually stale, the odor of sputum may become putrid from decomposition in the mouth or in the air passages (fetid bronchitis, bronchiectasis, lung gangrene). To people that come in contact with patients, there is no odor more trying than that of fetid sputum, unless it be that of bromidrosis!

(e) Consistence of the Sputum

This depends mainly upon the relative amount of mucus the sputum contains; in asthma, and sometimes in pneumonia, the sputum is so tenacious that it will not flow out of the sputum cup held upside down.

(f) Protein Content of Sputum

Sputum arising chiefly from increased secretion of the bronchial mucous membrane, as in asthma and in bronchitis, is poor in protein, whereas sputum arising in inflammations of the lung substance itself (pneumonia) or in transudations (pulmonary edema, chronic passive congestion) is more close to blood serum in its chemical composition and thus

is rich in protein. The amount of protein present in the sputum may therefore be helpful in differential diagnosis. One makes the test as follows (F. Müller):

Thirty to fifty cubic centimeters of sputum are placed in an Erlenmeyer flask, double the quantity of 1-per-cent aqueous solution of acetic acid is added, and the mixture well shaken. The acetic acid precipitates the mucin and leaves the proteins proper in solution. The mucin is filtered out, and a 10-per-cent solution of ferrocyanid of potassium added to the filtrate. An abundant precipitate indicates much protein and points to an inflammation of, or a transudate into, the lung.

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(*g*) *Amount of Sputum*

This is extremely variable. The largest amounts are met with (1) in certain bronchial affections (bronchoblenorrhea); (2) in large bronchiectatic or phthisical cavities (as much as one to two litres daily); (3) in pulmonary edema, or when abscesses or empyemas break into the bronchi. In such cases the sputum may be brought up in mouthfuls. In bronchiectasis the patients usually empty their cavities on changing their position after waking in the morning.

(*h*) *Larger Particles or Masses in the Sputum Recognizable by the Naked Eye*

(1) **Fragments.**—Occasionally, pieces of *lung tissue* (sequestra) are coughed up, in gangrene or in lung abscess. Pieces of *tumor* may appear in the sputum; the histological examination is important for diagnosis.

attacks, but Curschmann's spirals may occur also in patients that are not asthmatic, and, moreover, not all paroxysms of asthma are associated with

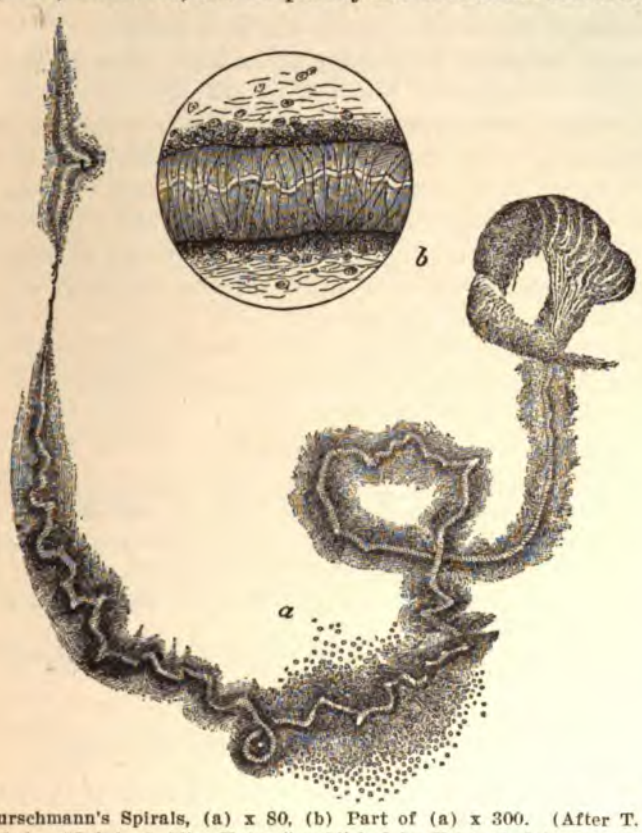

Fig. 158.—Curschmann's Spirals, (a) x 80, (b) Part of (a) x 300. (After T. Brugsch and A. Schittenhelm, "Lehrb. d. klin. Unter.," published by Urban & Schwarzenberg, Berlin.)

the expectoration of spirals. They can usually be found with the naked eye if one look for sagolike lumps of mucus, but one can scarcely be certain of them with the naked eye and the macroscopic examination should be controlled with the microscope.

(4) **Tuberculous Lenses.**—In the sputum from phthisical cavities, little particles, occurring singly or in small groups, each the size of the head of a pin, of a grayish-white or grayish-yellow color, of rather firm consistency, and resembling crumbs of bread in their appearance, are often met with. These "lenses" contain large numbers of tubercle bacilli, and sometimes also networks of elastic fibers. They have their origin in the caseous walls of a cavity.

(5) **Dittrich's Plugs.**—In the decomposing sputum of putrid bronchitis, of bronchiectasis, and of lung gangrene, small yellowish-white masses, closely resembling the tuberculous lenses described above, are sometimes seen. They have a very penetrating, foul odor. They consist of tissue

particles, or of small pus masses, which have undergone decomposition in the lungs, or in the bronchi. Microscopically, they contain numerous fatty-acid crystals and bacteria (cocci and long bacilli).

(6) **Fungus Colonies.**—These appear as small yellowish-white particles about the size of tuberculous lenses or of Dittrich's plugs, but of softer consistency. They are common (1) in pulmonary tuberculosis and in chronic bronchitis, where they are found microscopically to consist of masses of fungi; (2) in actinomycosis, then usually as the so-called "sulphur bodies," in which the microscope reveals the typical ray-fungus; and (3) in pneumonic aspergillosis, and in other mycoses of the lung (*q. v.*).

(7) **Echinococcus Cysts.**—Echinococcus cysts, or pieces of them, may, occasionally, be met with in sputum.

(8) **Lung Stones.**—Occasionally, a small stone is found in sputum; most often, it is a portion of a calcified bronchial gland.

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(*i*) *Microscopic Study of the Sputum*

Microscopically, sputum is studied for: (1) cells; (2) elastic fibers; (3) crystals; and (4) bacteria and parasites.

To make preparations of sputum for microscopic examination, one spreads out a larger mass on a glass plate on a dark background, picks out suspicious particles from several areas, and, with a needle, places these on a glass slide and applies a cover slip, avoiding too great pressure in order not to destroy the characteristic constituents (spirals, crystals, etc.). If necessary to dilute the sputum, one may add a drop of physiological salt solution. The following examinations (i-iv) are made with fresh, unstained sputum.

i. Cells in the Sputum

Among the mucous threads, one finds, normally, some epithelial cells and a few white blood corpuscles.

Squamous epithelium arises from the mouth, the pharynx, or the outer portion of the larynx.

Cylindrical epithelium may come from the nose, the upper pharynx or from the larynx and bronchi; the cilia are usually invisible. Cylin-

drical cells are abundant in catarrh of the mucous membranes and in bronchial asthma.

Alveolar epithelial cells are round cells with a vesicular nucleus; the cells are a little larger than white blood corpuscles. Fat granules, coal particles, and myelin droplets may be seen within the protoplasm; the fat granules stain orange red on the addition of a drop of alcoholic solution of Sudan III; myelin does not stain. In chronic passive congestion of the lung (cardiac disease), such cells are numerous in the sputum, and they contain then also yellowish-brown granules of hemosiderin or hematoidin (so-called "heart-failure cells"); such cells are also present in the sputum after any form of bronchial or pulmonary hemorrhage, and do not necessarily, therefore, depend upon myocardial insufficiency.

White blood corpuscles of the polymorphonuclear neutrophil type are abundant in purulent sputum; their nuclei are easily made visible by the addition of a drop of a 1-per-cent solution of acetic acid. *Eosinophilic leukocytes* are abundant in the sputum of asthmatic patients, where they may make up 60 per cent of all the leukocytes present (F. Müller). They may also be abundant in certain forms of chronic bronchitis, and during periods of improvement in some cases of pulmonary tuberculosis. In searching for eosinophil cells in the sputum, one makes a smear, dries it in the air and then stains with Jenner's stain (eosinate of methylene blue), just as one stains a blood smear. The cells are also easily recognizable in fresh unstained sputum through the presence of large highly refractive granules in the protoplasm.

Lymphocytes may also be present in sputum, sometimes in large numbers. They are easily recognizable as small mononuclear elements, the nucleus being surrounded by a narrow rim of non-granular protoplasm.

Red blood corpuscles are present in the hemorrhagic sputa met with in bronchiectasis, pulmonary tuberculosis, lung tumor, etc.

Tumor cells are sometimes recognizable in the fresh sputum. In carcinomata and in sarcomata of the air passages and lungs, cells from the tumor are sometimes broken off and expectorated. It is rarely safe, however, to make a diagnosis of tumor from the sputum unless the tumor particles are large enough to harden, section, and stain for histological examination.

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ii. Elastic Fibers in Sputum

These are found in the sputum in all destructive diseases of the lungs, especially in pulmonary tuberculosis and in lung abscess; occasionally, they occur in the sputum in gangrene, though in the latter disease they are usually absent, since a ferment that dissolves them is present.

In searching for elastic fibers one chooses a suspicious particle of sputum (*e. g.*, a tuberculous lens), places it on a slide, and adds a drop of 10-per-cent KOH solution. Or one may mix 30 to 50 c.c. of sputum with an equal amount of the alkali and warm on the water bath until clear. The mixture is then allowed to sediment in a conical glass or is centrifugalized, and the sediment is examined microscopically. The elastic fibers are easily recognizable; they occur either singly or in networks corresponding to the alveoli; occasionally, sheets of elastic tissue, possibly arterial in origin, are seen. The fibers are uniform in diameter, present sharp outlines, are highly refractive, tend to curl up at the ends; they are often branched; pressure on the cover slip does not give rise to varicosities or to changes in caliber. They are thus easily distinguishable from fatty-acid crystals (*q. v.*). They may be stained differentially, if desired, either fresh by magenta, or, after fixation, by Weigert's elastic-fiber method, or by the orcin method used in histology.

iii. Crystals in Sputum

Several varieties of crystals are met with in different sputa. They include hematoidin crystals, fatty-acid crystals, amino-acid crystals, cholesterin crystals, and the so-called Charcot-Leyden crystals.

(1) **Hematoidin Crystals.**—These occur in the form of brownish-red nodules, rhombic plates, and sometimes as amorphous yellowish-brown granules, usually lying in bundles; they are most common after old hemorrhages in the lung, or after rupture of lung abscesses or of liver abscesses into the lung.

(2) **Fatty-acid Crystals.**—These appear as fine, curved, colorless nodules, which melt to form fat droplets on warming the slide. They are soluble in ether and in KOH; on pressing on the cover slip, varicosities appear in the crystals. They are most abundant in Dittrich's plugs (*q. v.*) of putrid bronchitis, of bronchiectasis, of lung abscess, and of gangrene.

PLATE IX

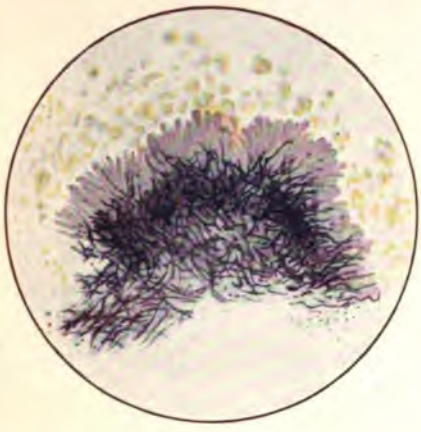

Fig. 1.—Actinomyces with Spores. (After Lenhartz, in L. Mohr u. R. Stachelin, "Handb. d. inner. Med.," published by J. Springer, Berlin.)

Fig. 2.—Actinomyces from the Sputum—Unstained. (After W. Kolle u. H. Hetsch, "Die experimentelle Bakteriologie, etc.," published by Urban & Schwarzenberg, Berlin.)

Fig. 3.—Cells in the Sputum—*a*, Alveolar Epithelial Cells Containing Coal Dust; *b*, Squamous Epithelial Cell; *c*, White Blood Cells; *d*, Cylindrical Epithelial Cell; *e* and *f*, Heart-failure Cells; *g*, Cells Showing a Peculiar Degeneration; *h*, Those with Myelin Droplets; *i*, One Full of Fat Droplets; *j*, Free Myelin; *k*, Red Blood Cells; *l*, Bacteria; *m*, Free Blood Pigment X 400. (After C. P. Emerson, "Clinical Diagnosis," published by J. B. Lippincott Co., Philadelphia.)

(3) **Amino-acid Crystals.**—In the sputum from pulmonary abscess, d in that from putrid bronchitis and from gangrene, one sometimes sees aracteristic crystals of leucin and of tyrosin. Such crystals arise as the sult of the action of proteolytic ferments.

(4) **Cholesterin Crystals.**—The characteristic large rhomboid plates of is secondary alcohol are occasionally seen in sputum along with amino-id crystals.

(5) **Charcot-Leyden Crystals.**—These are sharply-pointed, octahedral ystals, greatly variable in size, sometimes seen lying singly, or in oups, among the cellular elements the sputum. They are soluble in t water, in mineral acids, and in kalies. The crystals show an affin-y for eosin. They are very fragile, eing easily broken in making the reparation. They are most often iet with in asthmatic sputum where hey occur along with Curschmann's pirals and eosinophils. It has been uggested that the eosinophils sup-ly the material that gives rise to ie crystals; indeed, it seems very robable that they owe their origin o the disintegration of eosinophil ells. In searching for them, one icks out yellow specks or strips in ie sputum. Besides in asthma, they ave been observed in fibrinous bronchitis, in hay fever, and in distomiasis ulmonalis.

Fig. 159.—Charcot-Leyden Crystals—100/1. (After T. Brugsch and A. Schittenhelm, "Lehrb. d. klin. Unter.," published by Urban & Schwarzenberg, Berlin.)

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iv. Parasites as Seen in Fresh Sputum

Amebae, eggs of the lung fluke, and echinococcus hooklets, when present, are easily visible in unstained specimens; these are described below, also, under stained preparations.

v. Bacteria and Parasites as Seen in Stained Specimens of Sputum

Bacteria are always present in sputum. They are few in number in he pure mucous sputa of chronic bronchitis, of asthma, and of chronic

passive congestion, but they are present in large numbers in purulent sputa and in the various putrid sputa. In the former, staphylococci, streptococci, pneumococci and influenza bacilli are most often met with, while in the latter large anaërobic bacilli are also found.

The predominant organisms in the sputum may often be identified simply by examining a stained smear, but it is preferable to make also a culture from fresh sputum especially collected and washed with sterile salt solution for the purpose.

In making bacteriological cultures from the sputum, the following method is used: The patient is instructed how to expectorate from the lung into a sterile Petri dish. With a heavy sterile platinum needle, the examiner immediately picks out a ball of sputum and washes it in several successive Petri dishes containing sterile water or salt solution, in order to remove, as far as possible, bacterial contaminations from the mouth. Stained smears made before and after washing the sputum show the importance of this washing process (J. A. Luetscher). With sterile needles, the sputum mass is then broken up in a tube of bouillon, and a little bit, taken preferably from the center, is used for the making of cultures and of smear preparations. (For the media most suitable for the different bacteria suspected, see section on Diagnosis of the Infectious Diseases.)

The three bacterial forms in the sputum that are most important for clinical diagnosis are: (1) the tubercle bacillus; (2) the pneumococcus; and (3) the influenza bacillus. Other forms of vegetable microorganisms sometimes of importance here, include (4) the pyogenic cocci in lung abscesses and in bronchiectasis, (5) diphtheria bacilli, (6) streptothrix actinomyces and other forms of streptothrix, (7) aspergillus, (8) blastomyces, and (9) the thrush fungi.

Examination of Sputum for Tubercle Bacilli.—One chooses the more purulent part of the sputum, or looks for the tuberculous lenses. The bacilli are most abundant in the sputum that comes from the walls of cavities in the lung. (For the preparation of cover slips, and for methods of staining, see section on the Diagnosis of the Infectious Diseases.)

Examination of Sputum for Pneumococci.—These may be present in small numbers in Gram-stained specimens of almost any sputum examined. They are very numerous and are usually present in pure culture in the carefully collected rusty sputum of croupous pneumonia. They appear as lanceolate diplococci, often encapsulated. They may be isolated by cultural methods (*q. v.*) and their pathogenicity tested by inoculation of mice (at the root of the tail), or of rabbits (injection into ear-vein).

Examination of Sputum for Influenza Bacilli.—These extremely minute, polar-staining, bacilli occur usually in large masses when they are present in the sputum. Though in cover-slip preparations, stained by car-

Fig. 1.—Smear from Pneumonic Sputum, Stained with Dilute Carbolfuchsin. (After W. Kolle u. H. Hetsch, "Die experimentelle Bakteriologie, etc.," published by Urban & Schwarzenberg, Berlin.)

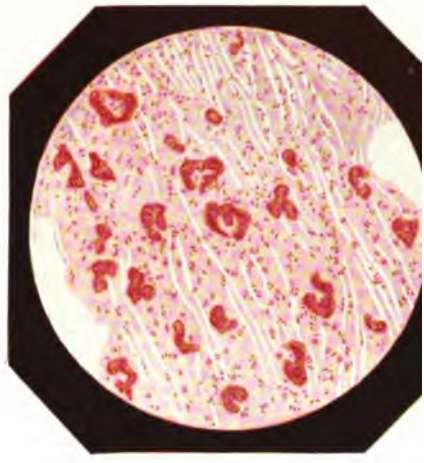

Fig. 2.—Bacillus influenzae from Nasal S
cretion. Fuchsin Stain. (After
Kolle u. H. Hetsch, "Die experimente
Bakteriologie, etc.," published by Urb
& Schwarzenberg, Berlin.)

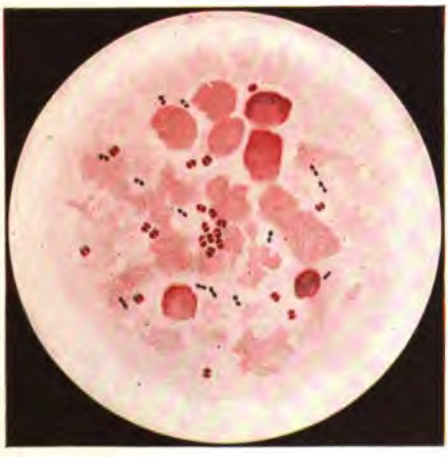

Fig. 3. — Micrococcus catarrhalis—Gram-fuchsin Stain. (After N. v. Jagic u. H. K. Barrenschen, "Atlas u. Grund. d. Klin. d. Mikroskopie," published by M. Perles, Wien.)

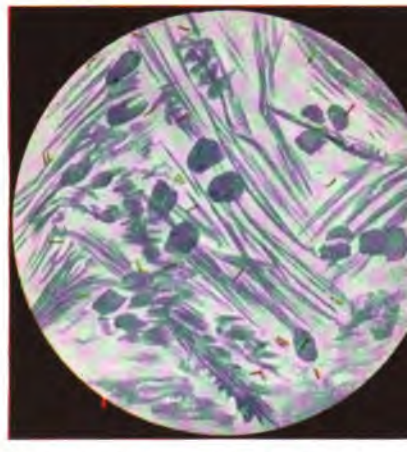

Fig. 4.—Tubercle bacilli. Stained w
Fuchsin and Methylene Blue. (After
v. Jagic u. H. K. Barrenschen, "Atlas
Grund. d. Klin. d. Mikroskopie," p
lished by M. Perles, Wien.)

bolfuchsin diluted with 10 parts of distilled water and allowed to act for 10 minutes, their nature may be suspected; the proof of their identity should be brought by means of cultures made upon blood-agar.

Examination of Sputum for Fungi.—Of the fungi met with in sputum, three varieties are of especial importance, (1) actinomyces, (2) aspergillus, and (3) blastomyces.

Streptothrix actinomyces.—In actinomycosis of the lungs, the sputum is sometimes glairy and mucilaginous, more often purulent, and contains yellow granules about the size of a small pin-head or of a sand-grain—the so-called "sulphur granules." The yellow color may not be visible except under the low power of the microscope; to the naked eye the particles may look grayish white. If one of these particles be placed on a glass slide, under a cover glass, and pressure be applied, one can see under the high power a central area consisting of fine, closely aggregated fungous threads, and a peripheral area, made up of branched, flask-shaped and clublike processes. Staining is unnecessary for recognition, but the fungus is brought out very beautifully if a little Lugol's solution be run under the cover slip. In dried-and-fixed smears, one may use methylene blue or Gram's stain for the mycelium, using safranin or carmin as a counterstain for the clubs.

Other Forms of Streptothrix.—Recently streptothrix infections of the lung resembling pulmonary tuberculosis have been reported, and forms of streptothrix have been found in the sputum during life and in the lesions in the lung at autopsy (See Part IV).

Aspergillus.—In aspergillus infections (pneumonomycosis aspergillina) the characteristic doubly-contoured threads (usually unbranched) containing numerous brownish pigmented spores are found. They are best seen on treatment of the sputum with 10-per-cent KOH. The fungus occasionally occurs in bronchiectatic, and in tuberculous, cavities.

Blastomyces.—This parasite is occasionally met with in the sputum in cases of systemic blastomycosis or oidiomycosis (*q. v.*). It is best brought out by treating fresh sputum with dilute KOH, when the doubly-contoured refractive yeastlike bodies become visible. If budding forms are seen, the fungus is probably a true *Blastomyces;* if endosporulation be visible, it is probably the fungus of coccidioidal granuloma (See Part IV).

Animal Parasites in Sputum.—The three animal parasites most likely to be met with in sputum are: (1) echinococcus hooklets and scolices; (2) ova of the lung fluke; and (3) Entameba histolytica.

Echinococcus Scolices and Hooklets in Sputum.—Rarely primary in the air passages, echinococcus material occasionally reaches them by rupture of a cyst of the liver into the lung, and then portions of the membranes, degenerated scolices, or hooklets may be found in the sputum.

OF NIMUS WESTERMANI.—The lung fluke that causes para hemoptysis is, in America, a rare parasite, though it is not at all uncommon in Japan. When in Tokyo, in 1899, I was shown a typical case by Dr. K. Miura. In that country, when hemoptysis occurs, they always look for the presence of the eggs of this parasite. The eggs are brown and are about 0.1 mm. long and 0.05 mm. broad; there is a cover, or operculum, on the blunt end.

Fig. 160.—Egg of Paragonimus westermani from Sputum. 1,000/1. After Katsurada, in M. Braun's "Die thierischen Parasiten des Menschen," published by Bale Sons & Danielsson, London.)

ENTAMEBA HISTOLYTICA.—When amebic abscess of the liver breaks through into the lung, amebae may be found in the sputum. In a case, personally observed, the hepatic condition was not suspected until the actively motile parasites appeared in the sputum. The sputum should be obtained fresh, and should be examined on a warm stage; the amebae present the same appearance as when they occur in the feces. (See Amebic Dysentery.) It should not be forgotten that amebae may be present in the sputum in pyorrhea alveolaris, and that microscopically it may be impossible to distinguish between the entameba histolytica and the entameba buccalis.

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11. Cough

This is an important symptom in various nervous and inflammatory diseases of the respiratory passages. Cough consists of a forcible, explosive expiration, during which the glottis is first closed and then quickly opened. The air current passing between the vocal cords gives rise to a noise that is at first of high pitch, becoming lower as the glottis opens.

Cough is a defensive mechanism, helping to cleanse the larynx, the trachea, and the larger bronchi. It is a reflex act, the sensory limb of the arc running in the N. vagus. The center in the medulla oblongata lies close to the respiratory center.

Violent coughing can injure the elasticity of the lung, especially in its upper parts. It also exerts an important influence upon the circulation. Thus, on coughing, the intrathoracic pressure is increased, the inflow of venous blood is hindered, and the outflow of arterial blood is favored, so that the arterial pressure may momentarily be markedly increased. This sudden heightening of the blood pressure may lead to arterial rupture in atherosclerosis or in aortic aneurism; it accounts also for the conjunctival hemorrhages in whooping-cough.

According to the sputum brought up, a cough is said to be *dry* or *moist*. When nothing is expectorated, it is called an *empty cough* (*e. g.*, in cutaneous or in pleural irritation). The cough may have a very *metallic* ring when cavities within the thorax are set into sympathetic vibration. When the glottis is not completely closed, or when the expiratory force is feeble, the cough may be *devoid of clang* (laryngeal paralysis, emphysema).

A *hacking* or frequently-recurring feeble cough indicates continuous slight irritation; it is met with in chronic catarrh of the upper air passages, especially in incipient pulmonary tuberculosis. Violent paroxysms of coughing, difficult to allay, are common in convalescence from influenza. The so-called *goose cough* of aortic aneurism is characteristic, and should always arouse suspicion. The *whoop* of pertussis (*q. v.*) has only to be heard once to be, afterward, easily recognizable.

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12. Examinations of the Lungs, Pleurae and Diaphragm by Means of Röntgen Rays

Much progress has been made recently in the diagnosis of diseases of the respiratory organs by means of Röntgen rays. Röntgenoscopy (or fluoroscopy) and röntgenography are both employed. Stereoscopic genography of the thorax as worked out by Dunham, Wenckebach, others is especially helpful.

(*a*) *Röntgenoscopy of the Lungs*

In studying the lungs by means of Röntgen rays, it is best to with a general röntgenoscopic view, preferably by dorsoventral tra

mination, the tube being placed at the back of the patient and the fluorescent screen over the front of his thorax. One can then decide, whether to use röntgenography for the whole thorax, or for certain regions only (*e. g.*, hilus, medial portions of apex, etc.). In special cases, however, ventrodorsal transillumination as well as frontal and oblique transilluminations for röntgenoscopy may be helpful.

(*b*) *Röntgenography of the Lungs*

General View.—During the exposure of the plate, the patient may either sit or stand. A soft tube (say 3 Benoist-units, or 6 to 7 Wehnelt-units) is used, at a focal distance of 50-60 cm., the anticathode being placed opposite the spinous process of the 6th thoracic vertebra. In adults of average size, the time of exposition required is from 5 to 10 seconds. Excellent pictures can also be obtained by brief exposures, provided an intensifying screen be used.

In dorsoventral (sagittal) illumination, the arms may be folded over the plate-holder in front so as to displace the scapulae as far as possible to the sides. The exposure is made while the breath is held at the end of a *deep* inspiration; in this way, there is a maximal amount of air in the lung at the time of exposure, the intercostal spaces are widened, the diaphragm stands at a low level, and the best view possible of the lower parts of both lungs is obtained. The patient should practice taking and holding a few deep breaths before the exposure is made, and the operator should make sure that the instructions to be followed at the time of exposure are fully understood.

In women, the breasts should be displaced lateralward, and held there by pressure of the plate-holder; otherwise, they give rise to disturbing shadows over the lung areas. When the breasts are huge, it may be advantageous to use ventrodorsal, rather than dorsoventral, illumination.

Local Views.—To obtain sharp pictures with maximal differentiation of the structures in local areas in the lung, it is best to use small cones or tubes to cut off the peripheral rays. This method is especially useful in making exposures of the apex, or of a hilus, of one lung. Here the anticathode should stand over the first intercostal space, in order to avoid the covering of the latter in the negative by the shadow of the second rib. The center of the bundle of rays is directed toward the jugulum, the head being bent back as far as possible.

Recently, a special method of making *röntgenograms of the upper aperture of the thorax* has been devised (Hart and Harras). The patient lies prone, the head raised by a high sand-bag, and the chest supported by a flat cushion. Between this cushion and the neck and upper chest is placed an 18 x 24 plate, no plate-holder being used. The spine must be straight, the shoulder blades of the two sides equidistant from the plate, the head not laterally flexed nor rotated. The x-rays pass, from behind,

through a tube or cone, so directed that the lower aperture of the tube forms a plane parallel to that formed by the upper aperture of the thorax.

Stereoscopic Views of the Lungs.—For studying and precisely localizing cavities, calcifications, infiltrations and foreign bodies in the lungs, as well as for examining pleural effusions, empyemas, and the air sacs of pneumothorax, stereoscopic röntgenographic views are exceedingly helpful, and should be made use of much more often than is at present the custom. In no other way can such exact information be arrived at regarding the spatial relations of intrathoracic lesions; the situation of a cavity, for example, can be precisely determined not only in the lateral but also in the anteroposterior direction. The technic of stereoscopic work has already been described in the section dealing with Examinations with Röntgen Rays.

(c) *Appearances of the Thorax, Lungs, Pleurae, Diaphragm, etc., on X-Ray Examination*

The student should early familiarize himself with the appearances presented by the lungs and other organs in the thorax on röntgenoscopy and on röntgenography.

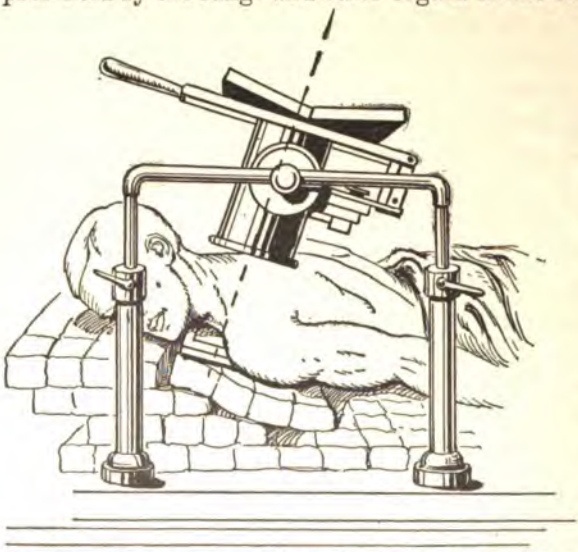

Fig. 161.—Diagram Illustrating the Mode of Making a Röntgenogram of the Apices of the Lungs and the Superior Aperture of the Thorax. (After C. Hart and P. Harrass, "Der Thorax phtisicus, etc.," published by F. Enke, Stuttgart.)

One view only can be described here; namely, that on dorsoventral transillumination. The two large clear areas (**lung areas**) are separated from one another by the median shadow (cardiovascular stripe); they are bounded above and at the sides by the shadows of the soft parts and the bones, and below by the two convex shadows that correspond to the two halves of the diaphragm.

The median shadow (**cardiovascular stripe**) is due to the sternum, the heart and the great vessels, the mediastina, and the spine. In the upper third of this median shadow, a lighter stripe may be seen corresponding to the air-containing trachea. The cardiovascular stripe will be described in detail under the Circulatory System.

The shadow of the right half of the **diaphragm** is ordinarily on a little higher level, is more intense, and moves less on respiration than that of the left half. The pulsating part of the cardiovascular stripe (apex of the heart) goes over into the shadow of the left half of the diaphragm; sometimes, in the latter, one can make out a clear area due to gas in the stomach (so-called "stomach bubble").

The **ribs** are seen as dark bands crossing the clear lung areas; the posterior portions of the ribs, concave below, are more distinct; the anterior portions, with convexity downward, are less distinct.

The **scapula** is visible on each side as a light triangular shadow. The **clavicles** yield a deeper shadow extending lateralward and slightly downward from the median shadow. Lateralward and below, the edge of the M. latissimus dorsi is usually easily visible.

In the upright position, the apices of the lungs may be obscured by the shadows of the first rib and of the clavicle, in which event it is necessary to change the position slightly or to move the clavicles, so as to make the apices accessible to observation.

Normal Appearance of the Lung Area.—Even normally, certain shadows, due to the variable concentration of the tissues (lymph glands, bronchi, blood vessels) within the lung, appear in the otherwise clear lung area, giving it a mottled, or networklike, appearance. These are normally most abundant near the hilus. They radiate out from it, and decrease in intensity, and in number, as the periphery of the lung is approached.

The hilus, itself, yields a crescentic shadow on each side with processes of varying intensity running out radially from it. The whole of this hilus-crescent is visible on the right side, but only a part of it can be seen on the left.

Beneath the hilus-crescent on each side is a shadow passing downward to the diaphragm known as the "companion-shadow of the heart" (v. Scriegen). That on the right side is usually separated from the heart-shadow proper by a narrow clear zone.

The clearness of the lung area depends, on the one hand, on the hardness of the tube used and the intensity of its rays, and, on the other hand, on the air content of the lung, the phase of respiration, the obesity, and the muscularity of the patient.

Situation, Form and Motility of the Diaphragm.—The form and position of the diaphragm depend upon the state of the thorax and of the thoracic and the abdominal viscera; the rib-level of the diaphragm is of relatively little significance.

The motility can easily be observed through the fluoroscope. On quiet breathing, there is a movement of 1-3 cm. on each side, while on deep breathing it may amount to 5-7 cm., the right side, however, usually descending somewhat less than the left.

Bilateral elevation of the shadow of the diaphragm occurs when the

abdomen is distended (ascites, tympanites, pregnancy, tumors, obesity). That faulty notions may be yielded by percussion is well demonstrated by x-ray examination.

Unilateral elevation of the diaphragmatic shadow is found: (1) in unilateral retraction of the lung (mobility also lessened); (2) in unilateral paralysis of the diaphragm; (3) in congenital atrophy of the diaphragm (on the left side); (4) in subphrenic abscess (lessened, or abolished, mobility); and (5) sometimes in hemiplegia.

Bilateral depression of the diaphragmatic shadow is met with (1) in emphysema and in rigid thorax (with lessened mobility); (2) in some asthmatic paroxysms; (3) in bilateral pleural effusion; (4) and in laryngeal stenosis.

Unilateral depression of the diaphragmatic shadow is met with (1) in unilateral pleural effusions (with lessened mobility); (2) in unilateral pneumothorax (extremely low position, shadow flat and immobile); and (3) in some acute asthmatic attacks, with loss of mobility.

Abnormal respiratory mobility of the diaphragm is met with in various states. In incipient apical tuberculosis, the movement of the half of the diaphragm corresponding to the diseased side sometimes lags behind the other half on respiration (F. H. Williams). In serothorax, in hemothorax, and on pyopneumothorax, if the fluid be not thick, its surface may be seen to rise on inspiration and to fall on expiration (paradoxical diaphragmatic movement of Kienboeck). Opinions differ as to the reasons for this.

Abnormal forms of diaphragmatic shadow may be seen, on deep inspiration, when pleuritic or pleuropericardial adhesions exist (angular notchings, wavelike curves).

Appearances in the Lung Areas in Pathological States.—Pathological changes in the lungs are recognizable in x-ray pictures as an increase or a decrease in the clearness in the lung areas, either diffusely over the whole lung, or involving larger or smaller circumscribed areas.

In *emphysema,* for example, the whole lung area on each side is abnormally clear, while in *chronic passive congestion* (cardiac decompensation), owing to the increased consistence of the lung, the areas are everywhere less clear than normal.

Circumscribed lung shadows indicate the presence of *solidifications,* or of *exudations,* in the lungs, or of *fluid* or of *thickenings* in the pleurae.

Nodules in the lung must be of a certain size in order to cast visible x-ray shadows. The exact position of a nodule is best shown by stereoscopic pictures. Fluoroscopic examination of lung shadows is useful only for the more extensive lesions; for finer changes, x-ray photographs (röntgenograms), taken while the breath is held, are necessary.

The changes in the x-ray picture characteristic of various pathological states will be described under the several diseases.

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SECTION II

SPECIAL DIAGNOSIS OF THE MORE IMPORTANT DISEASES OF THE RESPIRATORY SYSTEM

A. Diagnosis of the Principal Diseases of the Nose

We can refer here only to (1) certain inflammations (acute, chronic and specific), (2) epistaxis, (3) foreign bodies and parasites, and (4) the most common tumors (including polypi). Mention will also be made of (5) deflections of the nasal septum, and (6) nasal hydrorrhea.

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1. Inflammatory Diseases of the Nose (Rhinitis)

(*a*) *Acute Rhinitis*

Under this heading may be considered: (1) the acute catarrhal form of acute rhinitis, (2) the purulent form of acute rhinitis, (3) the pseudomembranous form of acute rhinitis, and (4) hay fever.

i. Acute Catarrhal Rhinitis

(*Rhinitis catarrhalis acuta, Common Cold in the Head, Coryza*)

There is hyperemia and swelling of the nasal mucous membrane, together with the secretion of a thin, clear, strongly alkaline fluid containing swollen epithelial cells, leukocytes, and bacteria (few at first, abundant later). Usually we see redness, and, sometimes, erosion and scabbing of the anterior nares. Sometimes the inflammation extends to the paranasal sinuses or to the conjunctivae.

An acute catarrhal rhinitis may be *primary* (due to bacteria in the nose, exposure to cold predisposing to infection), or *secondary*, as a part of some general disease (influenza, measles, scarlet fever, etc.).* A mechanical or chemical rhinitis is sometimes seen (dust, irritating vapors, iodism).

Symptoms.—In the premonitory stage, the patient feels chilly, ill at ease, and "stuffy in the head"; he begins to sneeze, to have itching or prickling sensations in the nasal passages and in the eyes, and, perhaps, complains of headache, backache, and slight pains in the extremities. Anterior rhinoscopy reveals hyperemia of the nasal mucosa, and, a little later, a profuse serous discharge. The temperature undergoes slight elevation. The patient is soon forced to breathe through the mouth, which dries the throat and parches the tongue. On the second or third day the discharge thickens, becoming mucoid, then purulent; the general constitutional symptoms abate; by the end of a week or ten days, in uncomplicated cases, the attack is over.

Complications and Sequelae.—Paranasal sinusitis, laryngitis, otitis media, chronic nasal catarrh.

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* Typhoid fever is almost never ushered in by an acute rhinitis.

ii. Acute Purulent Rhinitis

(*Rhinitis purulenta acuta, Blennorrhea*)

In this condition, there is reddening, and swelling, of the nasal mucous membrane. The secretion is mucopurulent, or may consist of pure pus; it is often fetid. Erosions and scab formations at the anterior nares and on the upper lip are common. The secretion is often abundant, sometimes accumulating in the paranasal sinuses (empyema of sinus) and then often maintaining the inflammation for some time. (See Sinusitis.)

Etiology.—The origin is always bacterial (streptococci, pneumococci, staphylococci, meningococci, influenza bacilli, etc.). Certain predisposing factors should be kept in mind (foreign bodies, tumors, infectious granulomata).

Complications.—There may be an extension (1) to the pharynx and to the larynx (pharyngitis, laryngitis); (2) through the eustachian tube to the middle ear (otitis media); or (3) through the lymph sheaths of the Nervi olfactorii to the cranial cavity (meningitis). The disease may go on to a chronic purulent or to an atrophic stage. (See Ozena.)

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iii. Acute Pseudomembranous Rhinitis

(*Rhinitis pseudomembranacea*)

Here, a yellowish-white or greenish deposit, more or less adherent, can be seen upon the swollen, reddened mucous membrane; it can be pulled off in shreds, or as a definite false membrane. It may be due to infection with streptococci, pneumococci or diphtheria bacilli (bacteriological examination).

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iv. Hay Fever

Definition.—A more or less severe inflammation of the mucous membranes of the nose, throat, and bronchi, occurring in susceptible persons in the spring or in the autumn, and caused by the inhalation of pollens of certain plants.

Historical.—The disease was formerly believed to be a neurosis. In 1873, Blackley pointed to the periodic occurrence of the affection, and established a relationship to the prevalence of certain pollens in the air at these periods. A most careful scientific study of the relations of pollens to the disease has been made by Dunbar.

Etiology.—The albumins of certain pollens act as intense irritants to the respiratory mucosa of certain susceptible people. Quantities of the isolated albumin of the pollen as small as one forty-thousandth of a milligram can yield a reaction in sensitive persons. The condition is almost certainly one of anaphylaxis, at least in part.

There are two periods in which hay fever is prevalent, the spring (early June) and the early autumn (middle or late August); the hay fever occurring in the spring is known as Vernal Hay Fever, June Cold, Rose Fever, or European Hay Fever, that occurring in the late summer and autumn as Autumnal Catarrh, or North American Hay Fever.

In the spring, the pollens of the *Graminae* and of the *Cyperaceae* are toxic, as are also those of privet, lily of the valley, thistle, swamp-pink, hairy Solomon's Seal, rape, green cabbage, and spinach.

In the autumn, the pollens of the *Ambrosiaceae* (rag-weed) and of the *Solidago* (golden-rod family) are most important; in addition, those of asters, chrysanthemums, daisies, and blue-bottles appear to be active.

Why some persons are susceptible to pollens and others not is still a mystery. Among hay fever sufferers, there are marked differences in susceptibility to the several pollens; some are sensitive to one kind of pollen only, others to a variety of pollens. Those that suffer in the spring are often immune in the autumn and *vice versa;* a few are susceptible to both the vernal and the estivo-autumnal pollens.

The disease often causes marked depression and other nervous symptoms, but it is no more prevalent among persons generally psychoneurotic than among others. Nor has the disease any relation to local abnormalities of the nose, such as enlarged turbinates.

Symptoms.—In affected persons, the disease comes on about the same time every year, corresponding to the period when the pollen concerned is present in the inspired air. After a day or two of slight nasal and conjunctival irritation with sneezing, a severe coryza develops; there is itching and burning of the nose, eyes, and larynx with profuse serous nasal discharge requiring the constant use of handkerchiefs in relays. The nose soon becomes obstructed, preventing nasal breathing; inspection thro

a speculum reveals swollen, intensely hyperemic conchae, which can temporarily be shrunken with an epinephrin spray, after which by palpation with a blunt probe hypersensitive areas on the anterior extremities of the conchae and on the septum, may, if desired, be marked out. The conjunctival and laryngeal symptoms are often marked; not a few patients suffer from distressing attacks of bronchial asthma at the height of their hay fever. The constitutional symptoms (headache, malaise, general weakness, palpitation, insomnia, mental depression) vary considerably in different cases. Autumnal attacks end after a hard frost.

The sneezing reflex is often set free by exposure to bright sun-light.

Patients that spend the hay fever season in regions free from the causative pollens remain free from attacks. Thus those that suffer from the autumnal type are free from the disease while on the ocean (far enough from shore), or while in Europe where there is practically no rag-weed or golden-rod. In the United States, many patients are free from attacks in the White Mountains, especially at Bethlehem, N. H. The Hay Fever Association publishes a list of places suitable for sufferers.

A favorite resort for hay fever sufferers of both the United States and Canada is the Georgian Bay (among its 30,000 islands); other places, relatively immune, include Chester (Nova Scotia), Murray Bay (Quebec), Muskoka (Ontario), and Mackinac Island (Michigan). In the pine-woods on the divide in Northern Wisconsin (Trout Lake), many patients are entirely free from hay fever. In all places, the irritation is less when the wind blows off the water, than when there is a land-breeze, laden with pollen. Flowers in a living room or in a sleeping room may be provocative of an attack.

Patients compelled to live in pollenous districts during the hay fever periods should stay in-doors and avoid dust as much as possible. Experiments are being made with antitoxins (*pollantin*), and with prophylactic pollen-inoculations, but, thus far, with results not wholly satisfactory. Oppenheimer, Clowes and others advise testing the sensitiveness of the skin and mucous membranes to dilute solutions of proteins derived from various pollens in order to determine which pollen is responsible, and if possible to bring about anti-anaphylaxis by desensitizing methods. The physician should protect the hay fever patient from the useless nasal operations of overzealous surgical enthusiasts!

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(*b*) *Chronic Rhinitis*

Three forms may be distinguished: (1) chronic nasal catarrh; (2) chronic purulent rhinitis, and (3) chronic atrophic rhinitis.

i. Chronic Nasal Catarrh

(*Rhinitis catarrhalis chronica*)

There may be only slight redness and swelling of the nasal mucous membrane, often visible only in patches; the secretion is mucopurulent, and tenacious. This type of nasal catarrh is often an occupation disease, due to dust (city-dwellers, millers, stokers, stone-workers, screw-makers, etc.). It is predisposed to by anything that narrows the nasal passages, *e. g.*, a deflected septum.

ii. Chronic Purulent Rhinitis

(*Rhinitis purulenta chronica*)

This state often follows the acute purulent form of rhinitis. The mucous membrane is red and swollen; there is a long-continuing purulent secretion. The turbinated bones, and the mucosa over them, unde hyperplasia (protective or hyperplastic rhinitis). The mucous mem of the lower concha may be diffusely thickened, or may present caulif like excrescences; occasionally, the periosteum is thickened. Similar

liferations may occur in the paranasal sinuses. Closure of their openings leads to chronic empyemas of the sinuses, which may cause atrophy of the bony wall and extension of the suppuration into the nose, the orbit, the cranial cavity or the subcutaneous tissue. There is danger of meningitis, of sinus thrombosis and of cerebral abscess (see Sinus Disease).

iii. Chronic Atrophic Rhinitis

(Rhinitis chronica atrophica; Ozena)

This condition is usually the sequel of a hyperplastic rhinitis; the mucous membranes and the conchae waste away; the ciliated epithelium is replaced by flat epithelium; there is atrophy of the glands and widening of the nasal cavities; the scanty purulent secretion tends to accumulate in the form of greenish, dry scabs and crusts; decomposition of the secretions yields the foul odor characteristic of the disease (ozena).

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(c) *Specific Inflammations of the Nose*

The two more important ones are: (1) tuberculosis and (2) lues; the three less commonly met with are: (1) glanders, (2) leprosy, and (3) rhinoscleroma.

i. Nasal Tuberculosis

Three forms are met with:

(1) *Tuberculous ulcers,* in phthisical patients, usually in the nasopharynx; (2) *tuberculous granulomata,* broad-based tumors, most often occurring on the cartilaginous septum, occasionally presenting grayish-red ulcerating or fungous surfaces; these are not as a rule associated with pulmonary phthisis; and (3) *lupus,* usually occurring at the vestibule of the nose, or in the nasopharynx.

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ii. Nasal Syphilis

This may be congenital or acquired. Coryza, leading to a stubborn, chronic nasal catarrh, is often the first sign of *hereditary lues;* occasionally, ulceration of the septum occurs.

In *acquired nasal syphilis,* the lesions may be primary (external chancre), secondary (macules and papules on the mucous membrane), or tertiary (periosteal or perichondrial gummata, which quickly break down and give rise to syphilitic ozena; perforation of the septum). Later, saddle nose and internal deformations are common. The *Treponema pallidum* can often be demonstrated in the lesions, and the Wassermann

action is positive. Entirely similar pathological changes occur in the nose in tertiary yaws (gangosa, *q. v.*).

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2. Epistaxis

Hemorrhage from the nose (*epistaxis*) may result from hyperemia (active or passive), trauma, severe infection (especially typhoid), arterial hypertension (nephritis, atherosclerosis), or hemorrhagic diathesis (anemia, chlorosis, leukemia, scurvy, multiple telangiectasis, etc.); occasionally, it is due to vicarious menstruation. In severe cases, life may be endangered unless the bleeding vessel be obliterated by the application of the thermocautery or the nose be plugged both in front and behind. In every case the bleeding point should be sought for; it will be found most often on the anterior third of the cartilaginous part of the septum.

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3. Foreign Bodies and Parasites in the Nose

In children, buttons, beads, pins, coins, beans, peas, screws, etc., may be found lodged in the nasal passages above or below the inferior concha.

Rhinoliths are uncommon. Ascaris and oxyuris are occasionally present in the nose. In vagrants, fly larvae may fill the nostrils.

When the presence of a foreign body is suspected, the open nostril should be closed and the patient told to blow through. If this does not reveal the object, one may try blowing air into the free nostril with a Pollitzer bag. If the foreign body be tightly wedged in, one should locate it with the speculum under bright illumination, after which it may be possible to pass a delicate, blunt, hook-shaped sound around it. In looking for a foreign body, it is, in general, wise to avoid the use of forceps and to take care not to dislocate the foreign body backwards on account of the danger of its falling into the larynx. If blood clots are present and make inspection difficult, the passages may first be cleansed by an alkaline spray; when the soft parts are swollen, a spray of cocain (4 per cent) and epinephrin (0.1 per cent) may be used to shrink them.

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4. Tumors of the Nose; Nasal Polypi

The most common tumor of the nose is a fibroma, which occurs as a gelatinous, polypoid mass of variable size on the lateral wall. Polypi are often a sign of underlying disease of the paranasal sinuses. Hard fibromata (nasopharynx, paranasal sinuses), fibro-adenomata, and carcinomata are much rarer.

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5. Deflections and Distortions of the Nasal Septum

Occurrence.—Normally the septum should be vertical, dividing the nasal cavity into two equal parts. Slight deviations from the normal are of no importance, but in many persons there is a marked curving or bending to one side (*deflection of the septum*). The deflection may be (1) a gentle curve of the entire septum, (2) a wavy line of curvature involving most of the septum, or, (3) a sharp curve or a bend of a circumscribed area of the septum. Small projections from the surface of the septum are known as *nasal spurs;* a single spur or several spurs may be present.

The majority of septal deviations are developmental, depending either upon delayed dentition and irregular eruption of the incisor teeth, or upon failure of the hard palate to develop properly.

Symptoms.—Spurs or deflections that do not interfere with nasal function need no especial consideration, but if the lesion obstruct breathing, hinder the free flow of secretions from the paranasal sinuses into the nose, or cause irritation by coming into contact with the mucosa of the conchae, symptoms develop. These may consist of (1) a feeling of stuffiness in the nose due to obstruction, (2) matutinal frontal headache, (3) asthmatic attacks through reflex irritation, or (4) chronic nasal catarrh.

Diagnosis.—Any of the symptoms above mentioned should lead to a careful examination of the nose. On rhinoscopy, the abnormality of the septum will be easily visible, and in many cases secondary changes in the nasal mucosa or in the paranasal sinuses can be made out.

One of the definite advances of modern rhinology has been the introduction of the simple operation of submucous resection of the septum in these cases.

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6. Nasal Hydrorrhea; Rhinorrhea

In neurotic persons, attacks of watery discharge from the nose (*hydrorrhea*) are not uncommon. They are probably of vasomotor origin, and are sometimes described as attacks of *coryza vasomotoria.*

In some instances, known as *cerebrospinal rhinorrhea,* an actual flow of cerebrospinal fluid from the nose has been observed (L. Hektoen).

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B. Diagnoses of Diseases of the Paranasal Sinuses

1. General Remarks on the Diagnosis and Differential Diagnosis of Inflammatory Diseases of the Paranasal Sinuses

Before the application of the methods of transillumination and of röntgenography to the study of sinus disease, physicians had to depend for the diagnosis of these affections upon (1) the subjective symptoms, and (2) rhinoscopic examination. While these older methods are still of very great value and should be employed in every case, the introduction of the two newer methods above mentioned has revolutionized the clinical study of diseases of the paranasal sinuses and permits us to make diagnoses much more easily and certainly than formerly; very often, too, with their aid it is possible to avoid some of the intranasal diagnostic operations which were formerly necessary.

of the Skull Seen from Above. The Bony Walls of the Orbit, the Ethmoidal Cells and the o that the Mucous Membranes of the Paranasal Sinuses and the Periorbita Have Been Laid Bare. ations. (After A. Onodi, in "Ergebnisse der Chirurgie und Orthopädie," published by J. Springer,

For clinical purposes it is convenient to divide the paranasal sinuses into two series: (1) the **paranasal sinuses of the first series,** or those that empty into the middle meatus; this series includes the *maxillary sinus* or *antrum,* the *frontal sinus,* and the *anterior ethmoid labyrinth;* (2) the **paranasal sinuses of the second series,** namely, those whose cavities open into the olfactory fissure or superior meatus; to this series belong the *posterior ethmoid cells* and the *sphenoidal sinus.*

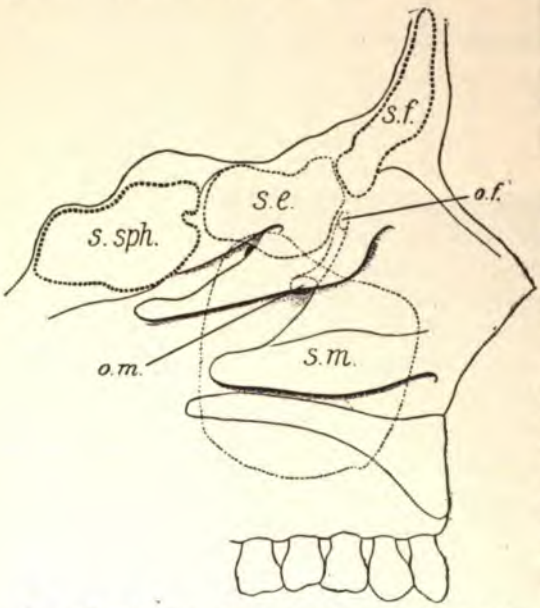

Fig. 163.—Diagram Showing the Relations of the Paranasal Sinuses to the Hiatus semilunaris. s.m.—Maxillary Sinus; s.f.—Frontal Sinus; s.e.—Ethmoidal Sinus; s.sph.—Sphenoidal Sinus; o.m.—Maxillary Ostium; o.f.—Frontal Ostium. (After M. Hajek, "Nebenhöhlen der Nase," published by F. Deuticke, Leipzig.)

If on rhinoscopic examination pus quickly reappear after the nose has been mechanically cleaned, the first question we ask ourselves is: Is the suppuration in a paranasal sinus belonging to the first series or to the second series? If the pus reappear in the middle meatus, either in front, below the anterior half of the middle concha, or, owing to obstruction to forward flow, behind, above the inferior concha, then we know that we must be dealing with a disease of the antrum, of the frontal sinus, or of the anterior ethmoidal labyrinth, or, possibly, with simultaneous involvement of two or three of the paranasal sinuses of the first series. If, on the contrary, the pus appear in front in the olfactory fissure, or in the superior meatus above the middle concha, we know it must come from one or both of the paranasal sinuses of the second series, that is, from the posterior ethmoidal cells or from the sphenoidal sinus.

The next step in the investigation is to decide upon the particular sinus in a series whence the pus is derived. In this connection, a few points may be emphasized:

(1) Disease of the maxillary sinus is by far the most common of the sinus diseases. With the patient in the upright position, the flow of pus from a maxillary sinus is usually intermittent, but the flow can be increased by inclination of the head forward; while the flow of pus from a frontal sinus is often continuous, and the outflow is diminished when the head is bent forward.

(2) X-ray examination and transillumination will reveal shadows in the affected sinuses; sinuses that are entirely clear on these two methods of examination rarely need further investigation.

(3) It is often possible to probe, or to irrigate, the maxillary sinus, either through the sinus maxillaris, or through an accessory opening. When this is not feasible, an exploratory puncture with a hollow needle can easily be made, when indicated, through the lateral wall of the inferior meatus, and the cavity washed out.

(4) If antral disease be excluded, and it is known that pus is being discharged into the middle meatus, it must come either from a frontal sinus, or from the anterior ethmoidal cells. To differentiate between these two sources, the x-ray examination often suffices, but it is sometimes necessary to remove the anterior portion of the middle concha and any polypi or hypertrophied mucous membrane in the neighborhood, after which the openings of the frontal sinus and of the anterior ethmoidal cells are accessible to rhinoscopic study. It must not be forgotten that when one paranasal sinus is diseased another may be simultaneously affected.

(5) In the differentiation between disease of the posterior ethmoidal cells and disease of the sphenoidal sinus, after the establishment of the fact that the discharge is into the olfactory fissure or superior meatus, and not into the middle meatus, we proceed by (a) making an x-ray examination, and (b) following the suppuration to its source, removing, when necessary, obstacles to the observation of this source by intranasal operation.

The general practitioner cannot be expected to command all the specialistic methods of examination required in the study of disease of the paranasal sinuses. He should, however, be familiar with the subjective symptoms and the complaints of patients that suffer from disease of these sinuses, and should be able to decide when it is necessary to call specialists to his aid.

Inflammations may extend to (1) the maxillary sinus, or antrum of Highmore, (2) the frontal sinus, (3) the ethmoid cells, or (4) the sphenoid cells.

Causes of Sinusitis.—These include primary infections of the mucous membrane in influenza, pneumonia, scarlet fever, measles, etc., and secondary infections by extension from the teeth (to the antrum), or as complications in tuberculosis, lues, trauma, etc.

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2. Maxillary Sinusitis

(Maxillary Antritis, Antrum Disease)

Definition.—An inflammation (catarrhal or suppurative) of the sinus maxillaris, due to infection, arising usually by extension from the nose, or from the root of a tooth, most often from the second bicuspid or the first molar tooth, the roots of which are nearest to the floor of the antrum.

Symptoms.—The patient may complain of a foul-smelling discharge from one side of the nose, or of pain, either directly over the antrum or radiating from it into the side of the face. If the pus has been swallowed for some time, there may be digestive disturbances or anemia; metastatic infections involving the kidneys or the joints are not uncommon complications. In one of Crowe's cases, the pus from an infected antrum had passed backward along the N. maxillaris into the skull cavity and given rise to an extradural abscess over the temporal lobes and to a meningitis. When the antritis is secondary to rhinitis, an examination of the nose will reveal the primary condition; when it is secondary to an infected tooth, there may be pain in the teeth on the affected side, and a dental röntgenogram may reveal the particular tooth at fault.

Transillumination of the antrum (*q. v.*) will reveal a shadow if there be an exudate in the antrum, if its walls be thickened, or if the cavity be filled by polypoid excrescences. Occasionally, a darkening is due to thickened bone or to the absence of an antrum on one side. Similarly, a röntgenogram of the two antra will reveal differences in density on the two sides. The x-ray photograph should be so taken that the frontal sinuses, the ethmoidal cells, and the antra of the two sides shall show on the same plate, as it is necessary to compare the two sides. The x-ray operator should avoid any superimposition of the foramen magnum and of the base of the skull over the antra.

Occasionally, after a menthol or a cocain spray, the antrum will be seen to drain into the nose (middle meatus); but sometimes it is necessary to open the antral wall, either through the nose, or from the mouth through

the alveolar process. In passing a trocar into the antrum, great caution should be observed, since examiners before now have passed it into the

Fig. 164.—Röntgenogram in Influenzal Inflammation of Antrum. E. P., Age 18—Infection of Right Antrum of About One Year's Duration Following an Attack of Influenza. Symptoms: General Lassitude, Occasional Headaches, Discharge in the Nasopharynx. Confirmed by Operation. Pure Culture of *B. influenzae*. (By courtesy of S. J. Crowe.)

orbit, or into the tissue on the far side of the antrum! When a chronic purulent condition has lasted for some time, fistula formation may occur, with necrosis of bone and the development of polypoid growths. It should not be forgotten that a purulent discharge originating in a frontal sinus or in the anterior ethmoidal cells may drain into an antrum, thus giving rise to a pyosinus.

Differential Diagnosis.—In ACUTE CASES, there may be swelling of the cheek, lip and eyelids on the affected side. One may at first suspect (1) *facial erysipelas,* but examination and the anamnesis should exclude it, since in erysipelas the swelling is in the skin itself, not in the deeper parts; the patient may have had several earlier attacks, and the swelling will have begun at the nose.

We next rule out (2) *furuncle of the upper lip* with infection of the facial veins; the anamnesis and the site of the original furuncle are usually decisive.

It is sometimes difficult to differentiate (3) a *maxillary periostitis* from an acute flare-up of antral disease; in both there may be swelling of the face, and tenderness on pressure in the canine fossa. But the anamneses differ; in ordinary periostitis, the patient will have had a preceding toothache, and on examination a carious tooth, or a tooth tender on pressure, will be found, while in acute maxillary sinusitis, a history of a preceding coryza or influenza will be elicitable; or if there is an exacerbation of chronic antral disease, there will be a history of periodic discharge of pus and perhaps of blood from the nose. The soft parts of the face are less swollen in sinus disease than in maxillary periostitis; the tenderness in the former is diffuse over the maxilla, reaching as far as the lower margin of the orbit, often accompanied by infra-orbital neuralgia, whereas in periostitis, the tenderness is most marked at the alveolar process of the upper jaw.

In CHRONIC CASES, rhinoscopy reveals hypertrophy of the mucosa of the middle concha, and often polypi in the nose. If there be no obstruction to the orifice of the sinus, the purulent outflow can be observed at times below the middle concha. When there is retention, transillumination and röntgenograms will reveal the darkened sinus.

Now and then, there is a possibility of confusing disease of the antrum with (4) *acute dacryocystitis,* in which there is swelling and tenderness in the naso-orbital angle. But in this case there will be epiphora, due to blocking of the lacrimal duct, and the patient will probably give a history of earlier attacks, and, perhaps, of previous treatment of the duct.

Other conditions, occasionally confused with antral disease, especially in children, are (5) *maxillary tuberculosis,* and (6) *acute parotitis.*

3. Frontal Sinusitis

The frontal sinus, on one or on both sides, may be the site of an acute catarrhal, or an acute purulent inflammation, or, more often still, of a chronic empyema. Occasionally, cysts, polyps, and hydrops of the cavities are met with. The sinuses are often the site of anatomical variation, as x-ray pictures show. The sinuses of the two sides are usually separated by a septum; either sinus may be subdivided into several compartments.

Symptoms.—On the subjective side, the local symptoms consist of headache and discharge from the nose; in some patients, there are complaints of disturbances of the sense of smell, obstruction of the nose, epistaxis, and eczema of the nostrils. The patients often present neurasthenic symptoms (incapacity for mental work, irritability, intolerance for alcohol and tobacco). Neuralgic pains in the domain of the N. ophthalmicus may occur. On the objective side, in suppurative disease of the frontal sinus,

the pus appears in the middle meatus, often under the anterior end of the middle concha. Sometimes polyps or hypertrophied mucosae prevent inspection of the most anterior part of the middle meatus. When this is not the case, removal of the pus with a swab will be followed by the appearance of a streak of pus running down from above and in front. When the patient sits upright the flow may be continuous, in contrast with the periodic flow in antrum disease. In latent stages, however, the flow need not be continuous; it is then most often visible in the early morning hours.

The continuous flow is often converted into a periodic flow through the presence of polypi or of hypertrophied mucous membrane. Such hyper-

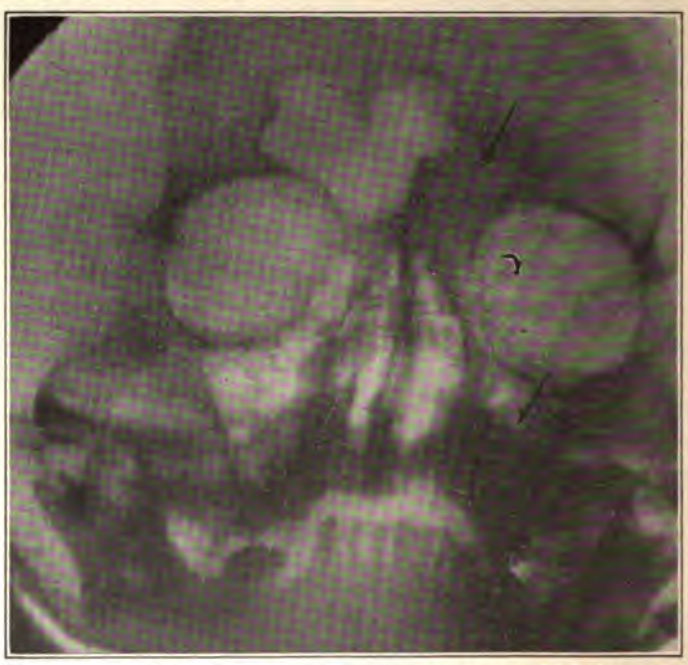

Fig. 165.—Röntgenogram Showing Clouding of Sinuses in Sinusitis. Patient, Age 30; Chronic Infection of the Right Frŏntal Sinus and the Right Antrum. Symptoms: Headache, Purulent Discharge, Nasal Obstruction, Indigestion (Hyperacidity). Confirmed by Operation. (By courtesy of S. J. Crowe.)

trophies usually involve the anterior end of the middle concha, and extend to the most anterior part of the hiatus and of the infundibulum, whereas in antral disease the polyps and hypertrophy are limited more to the posterior part of the hiatus in the immediate neighborhood of the ostium maxillare.

In disease of the frontal sinus, the most anterior part of the middle meatus is often narrowed on the diseased side owing to edema of the mucous membrane on the most anterior part of the concave side of the middle concha.

There is often tenderness over the anterior wall of the frontal sinus on percussion with the index finger, or with the percussion hammer. There may be tenderness on pressure at the root of the nose, on the orbital surface of the frontal sinus, especially at two spots; namely, (1) the inner upper angle of the orbit, and (2) the region behind the supra-orbital notch.

Occasionally, a slight edema of the soft parts of the forehead over the frontal sinus and of the upper eyelid can be made out; such an edema is prone to come and go; it is usually most marked in the morning.

Chronic infection of a frontal sinus occasionally gives rise to extradural abscess over the frontal lobe of the cerebrum and to meningitis.

Diagnosis.—This depends upon the history, the demonstration of increased discharge in the middle meatus of the nose, the exclusion of antrum disease, and upon the methods of transillumination and, especially, of x-ray examination of the sinuses. In some instances, the passage of a sound into the sinus and washing it out may be necessary; as a rule, such sounding should be avoided, since one may easily infect a healthy sinus, or may perforate the cribriform plate.

4. Ethmoidal Sinusitis

The ethmoid cells are divisible into two groups, an anterior and a posterior. The number of cells in each group is variable. It is important to remember that those of the anterior group chiefly empty into the middle meatus, and those of the posterior group for the most part into the superior meatus. Clinically, this division of the ethmoid cells into those that empty into the middle meatus and those that empty into the upper meatus is very convenient. The posterior group of cells stands in close relation to the nasal wall of the orbit, and, occasionally, an infection of the cells may lead to perforation of the orbital wall and give rise to unilateral exophthalmos and visual disturbances.

The ethmoid cells are often the site of inflammation, acute or chronic; the condition is, unfortunately, frequently overlooked.

Symptoms.—In latent cases, there may be no symptoms except those of a general run-down condition. In acute cases, and in acute exacerbations of chronic cases, there is usually headache, dull aching pain in the eyes and at the root of the nose, purulent discharge from the nose, disturbance of the sense of smell, nasal obstruction, and often secondary inflammations of the middle ears, tonsils, cervical glands, pharynx and larynx. The disease is sometimes the primary focus of infection in chronic arthritis; in all cases of chronic arthritis, the paranasal sinuses should be carefully examined. Various diseases of the eye and disturbances of the eye-muscles have been observed as sequelae of ethmoidal sinusitis.

Diagnosis.—Chronic empyema of the ethmoid cells includes many of

the cases formerly described as recurring polyp formation, and as fetid blennorrhea or ozena. Not infrequently the ethmoidal cells are involved simultaneously with other paranasal sinuses.

It is not uncommon to have one part of the ethmoid cells involved while the others remain healthy.

Occasionally, *mucocele* of the ethmoid develops, owing to retention of serum or mucus in the cells. It may appear as a mass, yielding parchmentlike crepitation. It should not be mistaken for a meningocele, a dermoid, or a neoplasm.

An empyema of the ethmoid cells may be either *open* or *closed*. In the open cases, the pus flows into the nasal cavity and polypi are common. In the closed cases, this flow of pus is prevented, owing to obstruction at the opening into the nose; the patient complains of headache; sometimes external swellings appear owing to dilatation of the cells; such swellings may project into the skull cavity or into the orbit.

In latent cases, the diagnosis can be made only by rhinoscopic study or by x-ray examination. In manifest cases, it may be suspected even in the absence of a rhinoscopic examination. Many patients complain of dryness of the throat, due to atrophy of the secreting glands of the pharynx. Whenever suspected, a careful rhinoscopic study should be made by a specialist, and an x-ray examination of the various paranasal sinuses resorted to. The x-ray is more helpful in the diagnosis of disease of the anterior group of ethmoidal cells than of disease of the posterior group.

The bulla ethmoidalis, situated just beneath the anterior end of the middle concha, is sometimes large and it may then look like a polyp; touched with a probe, however, it is found to be hard (bony), while a polyp is soft and mobile.

Operative measures on the ethmoid are especially dangerous, owing to the thinness of the lamina cribrosa, and to the fact that sheaths of dura surround the filaments of the olfactory nerves; meningitis has occurred after operation in a number of instances.

5. Sphenoidal Sinusitis

The sphenoidal sinus on either side is less often affected than the other sinuses, but it is sometimes the site of inflammatory changes, or of disease of its bony walls. The sinus is related anatomically to the N. opticus, the sinus cavernosus, the dura mater, and the A. c[illegible] the occasional complications of blindness from retrobulbar neur thrombosis, of meningitis, and of erosion of the A. carotis hemorrhage.

Symptoms.—The symptoms are very inconstant, but include h stiffness of the neck, nasopharyngeal catarrh, subjective disturban the sense of smell, vertigo, and general neurasthenic symptoms.

On objective examination, the discharge is found to empty either into the anterior part of the olfactory fissure, or, much more often, backward into the nasopharynx at the part of its roof that lies close to the superior meatus. It is sometimes associated with ozena.

The mucous membrane bounding the olfactory fissure becomes hypertrophied, and it is sometimes the site of polypi. Catarrhal inflammations of the pharynx and larynx are more common in sphenoidal sinusitis than in inflammations of the other paranasal sinuses. Occasionally, the bony walls of the sinus become diseased, in which event there is danger of cerebral complications (sudden unilateral blindness, due to compression of the optic nerve in the foramen opticum, or to perineuritis). Sometimes

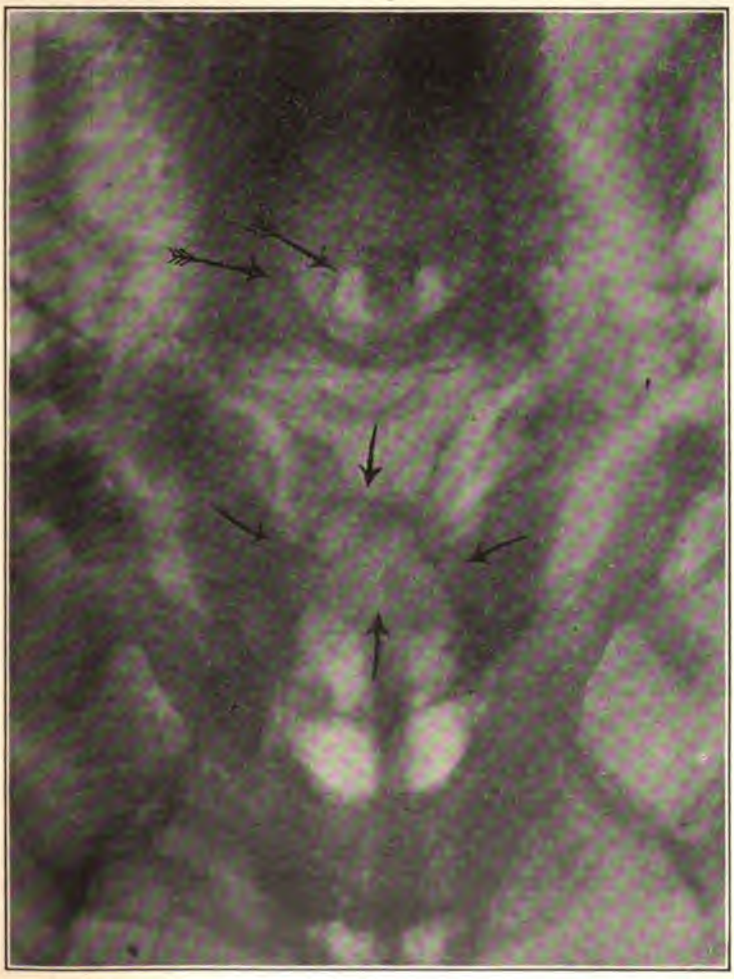

Fig. 166.—Method of Showing Right and Left Sphenoidal Sinuses. The Upper Arrows Point to the Foramen magnum and the Odontoid Process; the Four Lower Arrows to the Sinuses. (By courtesy of Drs. Baetjer and Waters, X-ray Dept., J. H. H.)

the retrobulbar tissues of the eye become invaded, with resulting exophthalmos. Occasionally, the lateral superior wall of the sinus is perforated, injuring the sinus cavernosus, and causing thrombosis or fatal hemorrhage.

Diagnosis.—The presence of pus in the olfactory fissure should excite suspicion; the nose should be thoroughly cleansed, and then be watched for the return of pus. The diagnosis may be aided (1) by x-ray examination, and (2) by the demonstration of the origin of the discharge from the sphenoidal cells, (a) by direct observation of the outflow from the opening of these cells, or (b) by the passage of a sound, and irrigation of the cells.

6. Mastoiditis

The mastoid is not a paranasal sinus, but an accessory cavity of the middle ear. For convenience, however, inflammation of the mastoid will be mentioned here. Secondary to otitis media, acute mastoiditis or mastoid disease frequently develops, and the condition should never be overlooked. Many cases when neglected go over into a suppurative process or into a chronic mastoiditis.

A purulent otitis media usually causes rupture of the drum with discharge to the outside. As long as the inflammation is confined strictly to the tympanic cavity, the main danger is impairment of hearing, but when it extends beyond this, serious complications often arise. Mastoiditis is, as a rule, the connecting link between purulent otitis media and its graver complications (Reik).

Symptoms.—Following upon the signs of an *acute otitis media* (local pain, fever, bulging of the ear drum, perforation, otorrhea), the pain may change its location and be assigned by the patient either to the region just over the mastoid, behind the ear, or to the depth of the ear itself. There is localized tenderness on firm pressure over the mastoid, or higher up over the mastoid antrum at the level of the upper border of the external auditory meatus. There may be no swelling nor redness; when these are observable over the mastoid, they indicate that the abscess has already broken through the bone and has given rise to a periostitis, or perhaps to a subperiosteal abscess. Another important sign of mastoiditis is swelling of the inner end of the posterior cutaneous wall of the external auditory canal, so that this portion droops just in front of the tympanic membrane. The posterior cervical lymph glands undergo enlargement. In acute mastoiditis there is fever, but in the chronic cases the temperature may be normal; there is a moderate leukocytosis.

Diagnosis.—Since otitis media is a common complication of scarlet fever, typhoid fever and influenza, the symptoms due to a developing mastoiditis are not infrequently attributed to the primary infection, the important local process being overlooked especially in children. In all

acute infections, especially in children, the mastoids should be regularly examined. Spontaneous pain, in or behind the ear, accompanied by tenderness over the mastoid is diagnostic, even in the absence of otorrhea and of local swelling or edema of the soft tissues over the mastoid.

In chronic otorrhea, an involvement of the mastoid by the chronic suppurative process is very common. Recently, x-ray examinations have been found helpful in the diagnosis of this condition.

Complications of Mastoiditis.—The intracranial complications are the

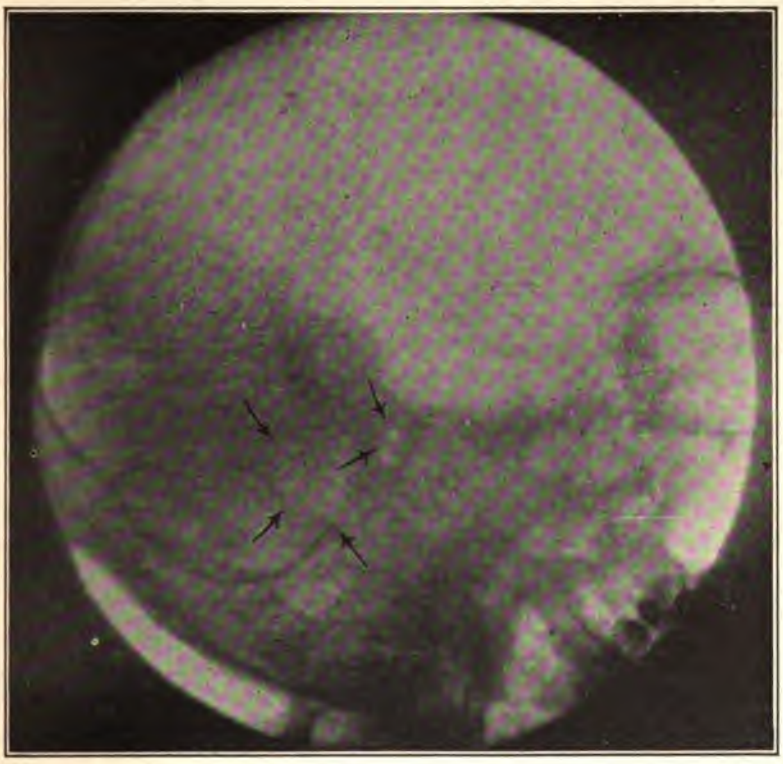

Fig. 167.—Röntgenogram of Mastoid Disease. The Large Clear Area (See Arrows) Near the Tip of the Left Mastoid Indicates the Situation of a Sequestrum and Extradural Abscess. (It Is Necessary in Taking an X-ray of the Mastoid to Have the External and Internal Auditory Meatus Superimposed—See Arrows, 2 Left Upper Ones.) In this Case the Right Mastoid Was Normal; Left Mastoid, Infection of Two Months' Duration. Pure Culture Streptococcus mucosus. Symptoms: Left-sided Headache, Purulent Discharge from the Ear, Local Tenderness Over the Mastoid, Edema of the Walls of the External Auditory Canal. X-ray Confirmed at Autopsy. (By courtesy of S. J. Crowe.)

most serious. Any one of the following may occur: (1) pachymeningitis, (2) extradural abscess, (3) leptomeningitis, (4) cerebral or cerebellar abscess, (5) thrombosis of the lateral sinus, or (6) purulent labyrinthitis.

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C. Diagnosis of Diseases of the Larynx

Four main groups of diseases of the larynx have to be considered:

1. Inflammatory (acute, chronic, specific);
2. Circulatory (edema of the glottis);
3. Paralytic;
4. Neoplastic (papillary fibro-epithelioma, fibroma, carcinoma);
5. Stenotic.

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[For other references, see under (1) Methods of Examination of the Larynx and (2) Diseases of the Nose.]

1. Inflammatory Diseases of the Larynx

These are met with especially in the members of certain professions: singers, lawyers, preachers, politicians, auctioneers. The use of alcohol and especially of tobacco predisposes.

(*a*) *Acute Laryngitis*

(Laryngitis acuta)

Two main forms are met with: a catarrhal and a diphtheritic.

i. Acute Catarrhal Laryngitis

(Laryngitis catarrhalis acuta, False Croup)

The attack comes on after "catching cold," with hoarseness, cough, and sometimes fever. On laryngoscopic examination, redness and swelling of the laryngeal mucous membrane is visible; occasionally, small erosions or hemorrhages can be seen. The secretion may be only slightly increased; it is mucous or mucopurulent.

In small children, an acute laryngitis may be associated with paroxysms of stenosis of the glottis, in the night; these attacks are known as "false croup." Waking suddenly, they startle their parents with the signs of an attack of suffocation; there is barking, crouplike cough, and difficult, whistling, inspiration, accompanied by retraction of the jugulum and of the epigastrium; expiration is also difficult and the voice is hoarse. After a short time, the respiration usually becomes easier; the acute symptoms pass off in a few hours, though the child may remain hoarse for several days. One must make absolutely sure at once that the child has not diphtheria; if there be any doubt, antitoxin should be administered. In false croup, intubation is occasionally, though very rarely, indicated.

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ii. Acute Pseudomembranous Laryngitis

(*Laryngitis pseudomembranacea, Diphtheritic Laryngitis, True Croup*)

The epiglottis is most often affected, but the whole laryngotracheal tube may be involved. The disease is rarely primary; it is usually secondary from the pharynx. A dirty, grayish-white, pseudomembrane (fibrin, leukocytes, necrotic epithelium) exists on the surface of the mucosa. The adjacent mucous membrane is deeply injected and swollen. Casts of the larynx and of the trachea are sometimes coughed up.

Etiology.—In most cases true croup is due to the diphtheria bacillus, though in the form complicating scarlet fever, measles, sepsis, etc., streptococci may be the cause. When a true false membrane is present in the pharynx, or larynx, antitoxin should be promptly administered without waiting for a bacteriological diagnosis. There is great danger of suffocation; intubation or tracheotomy may soon be indicated, and someone capable of performing them should be present with an outfit at hand.

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(*b*) *Chronic Laryngeal Catarrh*

(*Laryngitis catarrhalis chronica*)

Etiology.—The condition is most often due to chronic irritation from dust, smoke, etc. It is common in singers, public speakers, cigarette smokers, millers, stone-cutters, and metal-workers. It is sometimes secondary to nasopharyngitis or to pulmonary disease.

Symptoms.—The cough is often slight; the voice is feeble or hoarse, and tires easily, growing weaker on talking. On laryngoscopic e tion, one can make out moderate injection and swelling of the membrane. Often, visible thickenings of the epithelium of vocal cords can be made out; the horny layer becomes milk-v a dull blue color, is detachable with forceps, and often presents nodules (*pachydermia laryngis*); this is the condition in th "singer's nodes" (*trachoma of the vocal cords*).

The secretion from the larynx is tenacious and grayish-white in color; or it may be brownish, due to admixture of blood.

Diagnosis.—Before making the diagnosis of simple chronic laryngeal catarrh, one should exclude *tuberculosis* and *lues*, and should examine carefully the nose, the pharynx, and the lungs. Use may be made of the Wassermann reaction, the Calmette test, and, if necessary, of histological examination of a particle of tissue excised, for the differential diagnosis. The whole body should be carefully gone over in the search for signs of lues or of tuberculosis.

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(*c*) *Specific Inflammations of the Larynx*

These include the tuberculous, the syphilitic, the typhoidal and other specific inflammations.

i. Tuberculosis of the Larynx

(*Tuberculosis laryngis*)

The symptoms and signs are, at first, those of simple catarrh; they include hoarseness, cough, reddening of the mucous membrane, erosions, and paresis of the vocal muscles. Later, visible tuberculous infiltration develops, usually appearing first in the interarytenoid region; this subsequently breaks down to give rise to ulcers (flat, sharp margins; granular base). Sometimes, only a single ulcer develops; or two symmetrical ulcers may appear on the vocal cords; sometimes, there are several groups of confluent, "lenticular," ulcers. The edge of the epiglottis is often involved.

An *infiltrating form,* involving especially the adenoid tissue (epiglottis, aryepiglottic folds, vocal cords), giving rise to firm swelling, is sometimes seen. Later, caseation and ulceration occur; this form is often combined with arytenoid perichondritis.

A third form of tuberculous laryngitis is *lupus* of the larynx; small gray nodules with a red periphery appear; they do not undergo ulceration.

In advanced cases of laryngeal tuberculosis, there is pain on swallowing, and occasionally symptoms of stenosis.

The disease is nearly always secondary to pulmonary tuberculosis. About one-third of the patients suffering from pulmonary tuberculosis have also tuberculosis of the larynx. Primary tuberculosis of the larynx is exceedingly rare.

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ii. Syphilitic Laryngitis

(Laryngitis syphilitica, Laryngeal Lues)

Symptoms.—The voice is hoarse; there is sometimes actu
Cough and pain are slight, or absent. In secondary syphilis, th
picture may be that of subacute catarrh, accompanied by p

erosions. In the tertiary stage (more important), gummata may occur in any part of the larynx; in the trachea, they appear only at the bifurcation. Arising in the submucosa, or in the perichondrium, the gummata may form firm infiltrations, often narrowing the lumen. These infiltrations, breaking down, give rise to ulcers with firm, punched out, reddened margins. On healing, they leave white scars, which cause deformations (especially of the epiglottis), and often stenosis of the larynx, with permanent hoarseness. Ulceration and scar formation at the bifurcation of the trachea are not uncommon. It is important to recognize this condition before the retraction of the luetic infiltration has begun since in the later stages it is entirely resistant to ordinary specific treatment and not infrequently ends fatally through stenosis of the larynx.

Diagnosis.—The laryngeal picture is often characteristic. The anamnesis helps out. The occurrence of lesions elsewhere in the body should be looked for. The Wassermann reaction is positive.

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iii. Typhoidal Laryngitis

This is a rare complication of typhoid fever; the lymphoid tissue of the larynx, like that of the intestine, is affected and undergoes ulceration. In some cases, the laryngeal complication is a secondary infection due to other bacteria (cocci). Perichondritis is a frequent complication; both arytenoid cartilages were expectorated by one of my patients.

2. Circulatory Diseases of the Larynx

(*a*) *Edema of the Glottis*

Definition.—In this condition, a serous infiltration of the soft tissues of the larynx arises gradually, or, more often, suddenly, with suffocative phenomena (cyanosis, dyspnea). The soft tissues of the epiglottis, the aryepiglottic folds, and the false vocal cords are chiefly involved.

Occurrence.—It is met with most often in acute inflammations of the larynx or its neighborhood; it may occur also in the general anasarca of cardiopathies and nephropathies, and is then sometimes responsible for exitus. Rarely, edema glottidis is a fatal complication of angioneurotic

edema; occasionally, it occurs along with urticaria as a part of the "serum disease" following injection of antitoxin.

Symptoms.—There is a sudden appearance of dyspnea without apparent cause; it increases rapidly, the patient gasping for breath and quickly becoming cyanotic. There is aphonia. Expiration is easier than inspiration. The patient feels no pain. Unless relief is quickly obtained, death occurs from asphyxia.

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3. Paralytic Diseases of the Larynx

(*a*) *Paralyses of the Laryngeal Muscles*

To understand these, one must be acquainted with the muscles of the larynx and their functions, as well as their nerve supply.

The most important movements of the larynx are those determining the position of the vocal cords, that is, those altering the width and form of the vocal slit (rima glottidis). The vocal cords are farthest apart on deep inspiration, whereas they are closest together in the middle line on phonation. The change of position is brought about, mainly, by movement of the arytenoid cartilages; these can be moved away from the middle line, and can also be rotated on their perpendicular axes.

The Muscles of the Larynx

The three principal functions of the laryngeal muscles are:

(1) Closure of the glottis.

(2) Opening of the glottis.

(3) Tightening of the vocal cords.

Muscles closing the glottis: M. arytenoideus transversus, M. arytenoideus obliquus, M. crico-arytenoideus lateralis, M. thyro-arytenoideus (externus) and M. vocalis.

Muscles opening the glottis: M. crico-arytenoideus posterior.

Tensors of the vocal cords: M. cricothyroideus, M. thyro-arytenoideus internus (or M. vocalis).

The Nerves of the Larynx

The *nerves of the larynx* all arise from the N. vagus. The N. laryngeus superior supplies the mucous membrane of the upper half of the larynx as far as the margin of the vocal cords, the musculature of the epiglottis and the M. cricothyroideus, whereas the N. laryngeus inferior (or N. recurrens) innervates all the other laryngeal muscles (openers and closers of the glottis) and the mucous membrane downward from the vocal cords.

Complete Recurrens Paralysis.—The most important form of laryngeal paralysis is the so-called recurrens paralysis. It is sometimes bilateral, more often unilateral. All the laryngeal muscles except the M. crico-thyroideus are paralyzed, the vocal cords assuming the so-called "cadaveric" position, a sort of middle position, dependent entirely upon their elasticity and corresponding, approximately, to the position occupied during normal respiration (*i. e.*, midway between the phonation position and the inspiration position) (Fig. 168).

In *unilateral recurrens paralysis,* the healthy vocal cord is capable, on intonation, of crossing the median line and so closing the glottis. As a result, the voice is not aphonic, but only poor in clang.

The commonest *cause* of recurrens paralysis is injury of one or both nerves at the upper aperture of the thorax (aortic aneurism, carcinoma esophagi, mediastinal tumors). Occasionally, it is due to neuritis or to disease of the central nervous system (*e. g.*, bulbar paralysis).

Partial Recurrens Paralysis (*Posticus Paralysis*).—Among the fibers

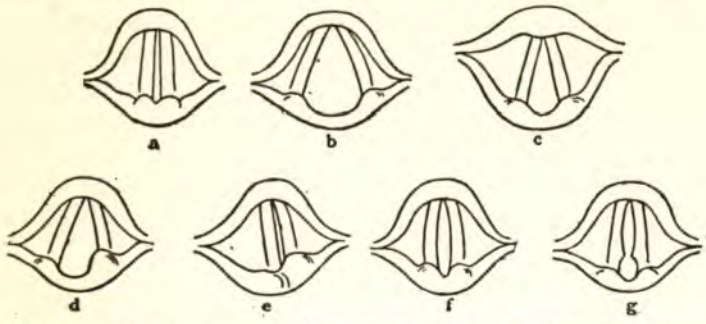

Fig. 168.—Diagrammatic Representation of the Position of the Vocal Cords in Different Forms of Laryngeal Paralysis. a and b—Normal Larynx; a—Phonation Position; b—Respiration Position; c—Cadaveric Position in Bilateral Recurrens Paralysis; d and e—Left-sided Recurrens Paralysis; d—Respiration Position; e—Phonation Position; f—Paralysis of the Tensors of the Vocal Cords; g—Paralysis of the Mm. Thyroarytenoidei and of the Mm. Interarytenoidei. (After Seifert & Müller, "Klin. Diagnostik," published by J. F. Bergmann, Wiesbaden.)

running in the N. recurrens are those supplying the M. crico-arytenoideus posterior (opener of the glottis), and these, of all the fibers of the nerve, are the most easily injured; thus, a recurrens paralysis always begins with "posticus paralysis," and, when recovery occurs from recurrens paralysis, the posticus muscle recovers its function last (Semon-Rosenbach law).

Bilateral posticus paralysis is a very dangerous condition, for, since the glottis cannot be opened, the stenosis results in inspiratory dyspnea, increasing to suffocation, though phonation is retained. The condition is not infrequently met with in postdiphtheritic neuritis.

Unilateral posticus paralysis causes standstill of the paralyzed cord

near the middle line, but since the other vocal cord is movable, there may be no clinical symptoms, and, unless a laryngoscopic examination be made, the lesion may go undiscovered.

A condition similar to bilateral posticus paralysis sometimes results from spasm and contracture of the adductor muscles.

Paralysis of the Adductor Muscles (*Closers of the Glottis*).—When the M. crico-arytenoideus lateralis and the M. interarytenoideus are paralyzed the vocal cord on the paralyzed side cannot be approximated to the middle line. In bilateral paralysis of these adductors, the vocal slit stands open, in the form of a large triangle; aphonia results, and coughing is unaccompanied by sound; respiration is normal.

In paralysis of the interarytenoid muscle alone, the arytenoid cartilages can be brought together in the region of the vocal processes, but not at their bases; on phonation, a triangular opening is then seen opposite the posterior third of the vocal cord. The voice is hoarse and there may be partial aphonia.

Paralysis of the Internal Thyro-arytenoid Muscle or Vocal Muscle.—This muscle is a tensor of the vocal cord, and paralysis of it leads to imperfect closure of the glottis on phonation, owing to insufficient tension of the vocal cord, which looks concave on the paralyzed side. If the paralysis be bilateral, one sees, on phonation, a lancet-shaped cleft between the cords. When the interarytenoids are simultaneously involved, the respiratory glottis remains open and the vocal processes project medialward; when the interarytenoids are not involved, the respiratory glottis closes normally.

Paralysis of the N. laryngeus superior.—Paralysis of this nerve causes unilateral immobility of the epiglottis, and anesthesia of the mucous membrane of the larynx (loss of reflexes, with "swallowing the wrong way"). Owing to the paralysis of the M. cricothyroideus, the vocal cord on the side of the lesion occupies a lower position than on the healthy side; the voice is deep, rough, and impure, and the patient cannot produce high tones.

Paralysis of the N. vagus as a Whole.—This gives rise, not only to the phenomena referable to the N. laryngeus inferior (recurrens) and the N. laryngeus superior, but also to paralysis of the muscles of the pharynx on the side of the lesion.

Hysterical Aphonia.—The aphonia here is usually due to a defective function of the adductor muscles; on attempting to phonate, the glottis is not closed. Cough, however, is accompanied by sound, showing that the glottis can be closed. This involvement of the function of speech without simultaneous involvement of the function of cough is characteristic of hysterical paralysis of the larynx.

The tensors of the vocal cords are often weakened in acute a
chronic laryngitis.

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4. Neoplasms of the Larynx

Tumors of the larynx may be *benign* or *malignant.* Benign growths include *singer's nodes, polyps,* and *papillomata,* though only the latter and some of the polyps are to be regarded as true tumors (neoplasms). Malignant growths of the larynx include *sarcomata* and especially *carcinomata.*

Symptoms of Tumors of Larynx.—These may be slight at first, but when present should lead to laryngoscopic examination. Hoarseness and tiring of the voice on use are, as a rule, the first symptoms. Cough is not common. Benign growths do not cause pain; malignant growths may excite pain, radiating to the ear of the affected side. Dysphagia may appear early in the course of a malignant growth. Dyspnea, continuous or paroxysmal, may accompany any kind of growth.

Inspection of Laryngeal Growths.—A thorough examination of all parts of the larynx should be made with the laryngoscope. The commonest site of neoplasm is at the anterior commissure of the vocal cords. If a growth be visible, we note its size, form, color, site, surface, consistency

(probe), mobility, attachments, and surroundings. If there be doubt as to the nature of the growth, a fragment should be excised for microscopical diagnosis.

In malignant growths, the tumor as a rule is not pedunculated; the neighboring tissues are red and infiltrated; there is early interference with the mobility of the vocal cord; the tumor bleeds easily and tends to ulcerate; dysphagia and dyspnea are complained of; and sometimes the regional lymph glands are enlarged.

(*a*) *Polyps of the Larynx*

These are very common. They appear as red, soft masses, usually situated on the anterior third of one vocal cord. They occur in adults of middle age, almost never in children. Histological examination of an excised fragment may be necessary for diagnosis. Once properly removed, such polypi do not tend to recur.

(*b*) *Papilloma of the Larynx*

Papilloma is rarer than polyp, but more common than other tumors of the larynx. It is met with most often in children, and appears as a cauliflowerlike excrescence, usually on one of the vocal cords. The cord moves normally. The growth shows no sign of ulceration or of inflammation. On removal, papilloma tends to recur, though it almost never undergoes malignant change. This tumor does not show histologically any areas of round-celled infiltration such as are seen in tubercle, lues, or singer's nodes; it differs from the papillary form of carcinoma, in that the latter bleeds easily, tends to ulcerate, and is associated with infiltration of the adjacent mucosa and with enlargement of the regional lymph glands. It is interesting that papilloma of the larynx, like papilloma of the bladder, can be satisfactorily treated with the high-frequency current.

(*c*) *Carcinoma of the Larynx*

Cancer usually begins on one of the vocal cords, occasionally on one of the false cords or in the ventricle, exceedingly rarely on the interarytenoid fold. It is rare before middle life.

Seen in the early stage, **intrinsic cancer of the larynx** appears as a small nodule on one vocal cord, bleeding easily, and tending to recur after removal. The histological diagnosis may not be easy, but if strands of epithelial cells invade surrounding tissue with no basal membrane, malignancy is certain. If allowed to remain, the tumor grows steadily, causes hoarseness and may ulcerate, though ulceration does not occur until the mass is twelve or eighteen months old. As it increases in size, it causes

dysphagia and dyspnea. In the late stages, the regional lymph glands and the base of the tongue may become involved. Metastases occur late.

By **extrinsic cancer of the larynx** is meant a cancer beginning in the epiglottis, on an arytenoid cartilage, in the recessus pyriformis, on an aryteno-epiglottidean fold, or on the pharyngeal surface of the posterior wall of the larynx. In this form, the early symptoms include *dysphagia* and *pain* radiating to the ear of the same side. The outlook is even graver than in intrinsic cancer.

(*d*) *Other Tumors of the Larynx*

These can only be mentioned here. They include *cysts, angiomata,* and *sarcomata.* Neoplasm may be simulated by leukemic nodules, by ingrowths of thyroid gland, by gummata, and by tuberculous nodules.

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5. Stenosis of the Larynx

Stenosis of the larynx and trachea may be due to (1) acute croupous or phlegmonous laryngitis, (2) gumma, (3) scars of earlier necrotic inflammations, (4) neoplasms, (5) aneurisms, or (6) foreign bodies.

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D. Diagnosis of the Principal Diseases of the Trachea and Bronchi

(*The Tracheopathies and the Bronchopathies*)

Here we have to deal especially with: 1, *inflammations* (tracheitis and bronchitis); 2, *dilatations* (bronchiectasias); and 3, *stenoses* (tracheal and bronchial stenoses).

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1. Inflammations of the Trachea and Bronchi

(*Tracheitis, Tracheobronchitis, Bronchitis*)

Of the acute inflammatory processes, the more important are (a) acute catarrhal tracheobronchitis, (b) acute capillary bronchitis (or bronchiolitis), and (c) acute fibrinous bronchitis. There are several forms of (d) chronic bronchitis. Closely allied, and therefore considered in this section, are (e) bronchial asthma and (f) acute anaphylactic shock; they are, however, neuromyogenic disturbances rather than inflammatory processes.

(*a*) *Acute Catarrhal Tracheobronchitis*

Etiology.—Three groups of factors may exert a causative influence: (1) *mechanical and chemical irritants,* like dust and gases, and certain drugs administered internally (*e. g.*, KI); (2) *infections,* some of them affecting the respiratory mucosa primarily (coryza, influenza, measles, pertussis), others affecting it secondarily (typhoid, lues, tuberculosis, diphtheria, etc.), and (3) *circulatory disturbances,* as in the various bronchial catarrhs due to stasis (cardiopathies, nephropathies, obesity).

Symptoms.—Here only the trachea and the larger bronchi are inv
The symptoms include cough, a feeling of tickling, tightness, bu

and soreness behind the sternum; there may or may not be slight fever, and slight expectoration.

The *sputum* is usually scanty in the beginning, and may be entirely absent; if there be any, it is thick, tenacious mucus; later, it usually becomes thinner, and generally mucopurulent. Cover-slip preparations and a sputum culture are desirable to determine the etiology (Bacillus influenzae, pneumococcus, streptococcus, staphylococcus, etc.). *The sputum should always be stained for tubercle bacilli,* especially when the physical signs are local, or when the sputum contains blood.

Physical Signs.—Inspection and percussion may be negative. On palpation, sometimes rhonchial fremitus can be felt. On auscultation, the breathing is vesicular and accompanied by coarse snoring sounds (sonorous rhonchi) over the upper chest, especially in the interscapular regions behind. If the medium sized and smaller bronchi become narrowed, from swelling of the mucous membrane and the accumulation of mucus, owing to extensions of the tracheobronchitis downwards, dry, piping, whistling sounds are heard (sibilant rhonchi). The condition then becomes one of diffuse bronchial catarrh (see below). As the bronchitis resolves and the secretion becomes more abundant and more fluid, moist, non-consonating, medium sized, or even bubbling, râles become audible. The abnormal sounds can then usually be heard over the whole thorax, though, as a rule, they are most numerous at the bases, behind. A *localized bronchitis,* especially if it be apical, is highly suggestive of tuberculosis, but influenzal infections sometimes give rise to similar signs.

Loud râles in the trachea, due to the accumulation of secretion there that remains unexpectorated, are often met with in agonal states (hence sometimes spoken of as the "death rattle").

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(*b*) *Acute Diffuse Bronchial Catarrh*

(*Capillary Bronchitis or Bronchiolitis*)

Definition.—A form of bronchitis, prone to occur in small children, in whom it is an extremely dangerous disease owing to the occlusion of

numerous small bronchioles by swelling of the mucous membrane, accumulation of secretion, and spasm of the walls.

Symptoms.—When due to cold or to stasis, there is usually only slight fever; when due to influenza or other specific infections, there may be high fever. The paroxysmal cough is distressing, and often causes tachycardia and pain in the side, the latter not being due to pleuritis, but to violent contractions of the muscles on coughing. The patients feel chilly and suffer from general malaise. The respirations are accelerated; there is marked dyspnea, and often cyanosis and sweating. On inspiration, the force may be insufficient to overcome the resistance, so that no new air can enter the alveoli; as a result, there is often extensive atelectasis (tympanitic percussion sound), with inspiratory retraction of the lower thorax in adults, and of the sternum in children. In other cases, the expiration may be too feeble to expel the air from the alveoli, in which event the air sacs become overdistended, the superficial cardiac dullness is diminished, and the lower limits of the lung come to occupy a lower level than normal on percussion.

The *sputum* is scanty at first, consisting of tough mucus (*sputum crudum*); later, it is thinner and more abundant (*sputum coctum*). In influenza, the sputum is often of a greenish color, and may be nummular, not unlike that from phthisical cavities. Stained smears and sputum cultures will reveal the etiological agent.

On auscultation, besides sibilant and sonorous rhonchi, there are many fine moist râles to be heard over both lungs. Vesicular breathing is enfeebled or roughened, and expiration is prolonged; the inspiratory and the expiratory sounds are absent over atelectatic areas.

Capillary bronchitis is often fatal, especially in young children. Bronchopneumonia is a common complication.

Diagnosis.—It is important, besides recognizing the bronchitis, to seek for an underlying disease (typhoid, pertussis, influenza).

Obliterating Bronchitis.—A rare form of involvement of the small bronchioles (bronchiolitis obliterans) sometimes follows aspiration of caustic vapors, which give rise to violent acute inflammation; the exudate undergoes organization, and leads to progressive obliteration of the bronchioles, and to death by slow asphyxiation.

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(c) *Acute Fibrinous Bronchitis*

(Pseudomembranous or Croupous Bronchitis)

Besides the form due to true diphtheria, an acute fibrinous bronc may occur in pneumonia or as a primary disease of chronic course unknown etiology ("essential form").

Symptoms.—An *acute* and a *chronic* form are distinguished. In both the patients cough up casts of the bronchial tree. Before expectoration of the cast, the breath sounds are enfeebled in the part of the lung affected, and expansion is diminished. There is marked cyanosis and dyspnea, sometimes attacks of suffocation. The normal sounds return after evacuation of the cast. The acute cases are serious, often ending fatally. Chronic membranous bronchitis may recur over long periods.

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(*d*) *Chronic Bronchitis*

Several forms are distinguished, among them: (1) **dry bronchitis (bronchitis sicca),** with scanty secretion of tough mucus; (2) **broncho-blennorrhea,** in which the sputum is abundant, thin, mucopurulent and separates, on standing, into three layers, just as in bronchiectasia; (3) **serous bronchorrhea,** or pituitous catarrh, in which the expectoration is fluid, seromucous, poor in protein, and very abundant (1 to 1½ liters in twenty-four hours). It is often accompanied by marked dyspnea, and is sometimes described as wet asthma (asthma humidum); and (4) **putrid or fetid bronchitis,** with abundant, stinking, purulent sputum, separating into three layers, and containing, in the bottom layer, Dittrich's plugs. When the bronchitis is due to stasis, the sputum contains many "heart-failure cells."

Etiology.—The disease is due, usually, to recurring attacks of acute bronchial catarrh, dependent upon inhalation of dust (mineral or vegetable), upon extension of inflammation from the nose or throat, or upon stasis in the pulmonary circulation as in cardiac and renal disease, in atherosclerosis, in emphysema, in cirrhosis of the lung, in kyphoscoliosis, and in certain metabolic diseases, especially obesity and gout. Certain families seem to be definitely predisposed.

Chronic bronchitis may also occur as an accompaniment of chronic infections of the lung (pneumococcus, tubercle bacillus), and of bronchiectasis.

Symptoms.—The patients are usually afebrile; they suffer from a chronic cough, worse in winter ("winter cough"), with more or less expectoration. The *physical signs* in chronic bronchitis vary according to the amount of the secretion; when it is scanty ("dry catarrh"), there are sibilant and sonorous rhonchi; when it is abundant, moist râles, of variable size, but non-consonating, are audible. The signs are present in both lungs and are most marked in the lower lobes. The different forms of chronic bronchitis are distinguishable by the characters of the sputum. (See above.) The patients are more or less cyanotic, and exhibit an

expiratory dyspnea. After the disease has lasted for some time, the patients all show signs of pulmonary emphysema. In this disease, the general state of the patient may not be much affected; in acute exacerbations, however, there may be fever and increased dyspnea. In such acute exacerbations it is common to find at one or both bases posteriorly an area of impaired resonance on percussion with a diminution in the breath sounds and numerous coarse râles; the presence of such evidence of a complicating hypostatic pneumonia should be especially looked for in older people.

Diagnosis.—An important clew lies in the fact that in uncomplicated chronic bronchitis, the physical signs indicate a diffuse involvement of both lungs, though they may be more marked in some parts than in others. One must carefully exclude tuberculosis (family history, stain for bacilli, physical study of apices, x-ray). The frequent association of chronic bronchitis with emphysema, with heart disease, and with nephritis should be kept in mind. Putrid bronchitis is commonest in association with bronchiectasia, and with pulmonary gangrene.

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(*e*) *Bronchial Asthma*

(*Asthma bronchiale; Nervous Asthma*)

Definition.—A condition in which paroxysmal attacks of marked dyspnea (chiefly expiratory) occur, due to sudden bronchospasm and to swelling of the bronchial mucous membrane, and apparently dependent sometimes upon a reflex neurosis, sometimes upon anaphylactic chemical stimulation of the autonomic nervous system.

Etiology.—Among the sites of irritation in the cases due to reflex neurosis may be mentioned (1) the nose, especially enlarged conchae and nasal polypi (nasal asthma); (2) the genitals (asthma sexuale), especially the uterus in the female, the posterior urethra in the male; and (3) the trachea and bronchi. Heredity plays an important rôle. Rickets and gout seem to be predisposing factors. The asthma due to hay fever has already been described.

In the anaphylactic cases, the patients seem to be susceptible to various proteins that act as "asthmogenic substances"; among these may be mentioned horse serum and egg albumen.

Symptoms.—During an attack, respiration is labored, though not necessarily accelerated; cyanosis and orthopnea are common. An acute pulmonary emphysema (*volumen pulmonum auctum*), with descent of the diaphragm, develops also during the attack.

Attacks are common at night; they usually last several hours, sometimes days.

In an attack, the lower limits of the lung are depressed and but little mobile; the superficial cardiac dullness is diminished; a boxlike tone is elicitable on percussion. The respiratory murmur is obscured by loud snoring and whistling sounds, especially during expiration. At the end of an attack, a tough mucus, containing Charcot-Leyden crystals, eosinophils, and Curschmann's spirals, may be expectorated. Inspiration may be roughened, and expiration prolonged, for a period after the subsidence of the attack; later, these signs and the rhonchi disappear. In long-standing cases, permanent pulmonary emphysema develops.

The disease is more common in men than in women, and in "nervous" people than in the phlegmatic.

Diagnosis.—True bronchial (or "neurogenic") asthma is to be distinguished (1) from *cardiac asthma;* (2) from the dyspnea of *emphysema;* (3) from *renal asthma;* (4) from *spasm of the glottis* (here the dyspnea is inspiratory, not expiratory); and (5) from *hysterical pseudo-asthma* (absence of cyanosis, violent thoracic movements, "barking").

In this country attention has been paid of late to bronchial asthma considered as an anaphylactic phenomenon. The matter has been discussed by Meltzer, by Matthews, by Koessler and others. Some asthmatic patients seem to be especially sensitive to certain proteins. One of my patients recently gave a sharp reaction to serum protein, another a violent reaction to milk protein. Many asthmatic patients are said to be sensitive to egg-white, a few to meat proteins. The tests for sensitization are easily made by intradermic injection of a minute quantity of the protein.

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2. Dilatation of the Bronchi

(*Bronchiectasia or Bronchiectasis*)

The bronchi may undergo (1) diffuse (cylindrical) dilatation, or (2) circumscribed (saccular, or spindle-shaped) dilatation; the condition is known as bronchiectasia or bronchiectasis. One, several, or all of the bronchi may be involved.

Etiology.—Bronchiectasias are usually the result of chronic inflammations that weaken the walls of the bronchi, diminishing their elasticity and increasing their distensibility. A localized form may follow those cicatricial processes in the lungs or pleura that lead to traction upon the walls of the bronchi from without (after pneumonia or pleurisy). A very important factor, in many cases, is *increased pressure within the lumen* of the bronchus through increased (expiratory) air pressure, or through accumulated secretions.

Cylindrical bronchiectasia is common in children after capillary bronchitis, bronchopneumonia or pertussis; in adults it is often a sequel to chronic bronchitis. Saccular bronchiectasia may be the sequel of a bronchiostenosis due to pressure from aneurism or neoplasm or to scars from ulceration of the bronchial wall in lues or in tuberculosis; occasionally it follows aspiration of a foreign body. In chronic indurative processes in the lung (*e. g.*, in Corrigan's pulmonary cirrhosis), and in thickened pleura, bronchiectasis sometimes develops.

Symptoms.—Paroxysmal cough, with expectoration by "mouthfuls" in the morning, especially on change of posture, is the characteristic diagnostic sign.

The *sputum* is abundant, and usually putrid (due to a complicating putrid bronchitis); it separates typically into three layers (frothy, serous, and purulent), the lowermost layer containing Dittrich's plugs. Tissue fragments are not present in the sputum in simple bronchiectasia; when found, they point to abscess, or to gangrene, of the lung. The albumin content of the sputum is not abnormally increased.

In the saccular form, the physical signs of a cavity (*q. v.*) may be dis-

tinguishable after expectoration. The auscultatory findings may differ markedly before and after expectoration. The persistence of râles in a definite area of the thorax often permits one to localize a bronchial dilatation in the absence of cavernous symptoms. Exquisite pictures of the bronchial tree on both sides, and of any dilatations existing, are obtainable by stereoscopic röntgenography.

There is, in cases of long standing bronchiectasis, a marked tendency to recurring attacks of acute infection of the diseased bronchi. In the more severe of these attacks there is considerable elevation of temperature, the amount of sputum in the first days may be diminished, and signs of bronchopneumonia appear over the portions of the lungs affected. Diffuse impairment of the percussion note is observed, and patches of tubular breathing and moist râles are found. The repetition of these acute attacks gives to the disease its progressive character.

Hemoptysis is common, and may, erroneously, excite the fear of tuberculosis. Bulbous enlargement of the finger-tips is often present in bronchiectasia. Röntgenograms show the change in the tips of the phalanges, and often also subperiosteal bony deposits along the shafts of the phalanges and metacarpal bones (toxicogenic osteoperiostitis).

Complications.—The accompanying putrid bronchitis may give rise to, or follow, *gangrene* of the lung. Metastatic infections (*brain abscess, arthritis*) are not so very uncommon as complications of bronchiectasia. Inflammatory *infiltrations of the parenchyma of the lung* near the cavity are common; occasionally *pleuritis* or *empyema* develops, the latter often becoming putrid.

Diagnosis.—Before the x-ray could be applied, diagnosis was often very difficult. Even now there may be difficulty, especially in the pure bronchitic forms with simply general cylindrical ectasia. In saccular ectasia, if cavity symptoms are present, the localization is easy through the physical signs and through stereoscopic röntgenograms; sometimes râles audible over a circumscribed area are the only localizing signs. The sputum raised by mouthfuls in the morning is often more decisive than the physical signs over the lungs. In ruling out tuberculosis, chronic lung abscess, and pulmonary gangrene, our diagnostic resources are sometimes taxed to the utmost; the same is true of liver abscess and of subphrenic abscess rupturing into the lung. A careful consideration of the anamnesis, the physical signs and the x-ray findings will usually permit us to arrive at a correct diagnosis. Bronchoscopy may be resorted to in doubtful cases, and probably should always be applied before advising surgical therapy.

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3. Stenosis of the Trachea and of the Bronchi

(*Tracheostenosis, Bronchiostenosis, Foreign Bodies in the Bronchi*)

Stenosis of the trachea or bronchi may result from (1) *inflammatory exudate* (*e. g.*, diphtheria, fibrinous bronchitis) or *cicatrix* (lues); (2) *foreign bodies,* especially in children (peas, beans, buttons, coins, bone), and in adults under anesthesia (tooth); and (3) *pressure from without* (aneurysm, goiter, carcinoma, enlarged glands, etc.).

The dyspnea is often extreme, with stridor on inspiration and on expiration. The diagnosis of bronchiostenosis depends upon (1) the anamnesis, (2) decreased movement of the affected side, and (3) enfeeblement of the respiratory murmur in the area supplied by the bronchus. When the cause of the bronchiostenosis is unknown, it may sometimes be discovered by röntgenography or by bronchoscopy (*q. v.*). Moreover, röntgenography and röntgenoscopy reveal a characteristic lung area in bronchiostenosis.

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E. Diagnosis of the Principal Diseases of the Lungs

(*The Pneumopathies*)

For clinical purposes the principal diseases of the lungs may be divided into five main groups:

1. Pneumopathies of inflammatory origin (pneumonias).
2. Pneumopathies due to alteration of the air content of the alveoli (atelectasis, emphysema).
3. Pneumopathies of circulatory origin.
4. Pneumopathies due to the presence of foreign bodies and of parasites.
5. Pneumopathies due to neoplasms (tumors of the lung).

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1. The Inflammatory Pneumopathies or Pneumonias

These are divisible into three great groups:

I. The parenchymatous pneumonias:
   (a) Genuine lobar pneumonia (fibrinous).
   (b) Lobular or bronchopneumonia (catarrhal).
   (c) Metastatic pneumonia (embolic).
   (d) Chronic pulmonary abscess and gangrene.
   (e) Gangrene of lung.

II. The interstitial pneumonias.

III. The "specific" pneumonic processes:
   (a) Tuberculous pneumonia.
   (b) Luetic pneumonia.
   (c) Actinomycotic pneumonia, etc.

I. THE PARENCHYMATOUS PNEUMONIAS

(*a*) *Genuine Lobar Pneumonia*

(*Fibrinous or Croupous Pneumonia*)

Definition.—An acute infectious disease of sudden onset (violent chill, high fever, tachypnea, and stitch in the side), usually without prodromata, and leading to consolidation of one or more lobes of the lung.

Etiology.—The disease is caused by infection with the pneumococcus (*Micrococcus lanceolatus*); rarely with the *Bacillus mucosus capsulatus*

(Friedländer's *pneumobacillus*). For the several strains of pneumococci concerned, see the Section on Infectious Diseases in which Cole and Dochez's work is referred to (Part IV).

The disease may occur at any time of year, but is commonest in the United States during the winter months. According to Keller, the incidence of lobar pneumonia is inversely proportional to the rain-fall. Conditions that predispose a person to the infection include exposure to cold and wet, trauma, and irritation of inhaled gases or dust. One that has once had an attack is likely to have another or several attacks later on in life. Children and old people are often affected. Women suffer less often than men. Contagion seems to play a part sometimes, especially in pneumonia epidemics.

Symptoms.—Clinically, lobar pneumonia runs its course in three stages:

1. The initial stage (corresponding histologically to the stage of ENGORGEMENT and of beginning infiltration).

2. The stage of demonstrable CONSOLIDATION of the lung tissue (corresponding histologically to red hepatization and gray hepatization).

3. The stage of CONVALESCENCE, with fall of temperature (often by crisis, sometimes by lysis) and return of the physical signs to normal (corresponding histologically to the stage of RESOLUTION, or absorption, of the exudate after autolysis).

On *inspection,* the patients usually look very ill. The respiration is accelerated (30-60 per minute) and shallow, partly owing to the pleural pain. There is cyanosis, marked dilation of the nostrils during respiration, coughing, and diminished expansion of the thorax on the side affected. The face is flushed but sometimes only on the side of the affected lung. The patient may lie on the affected side in order to lessen the pain by restricting movement.

On *palpation,* the vocal fremitus is increased over the affected lobe as long as the bronchus is patent. Expansion of the side affected is diminished. A friction fremitus due to the accompanying dry pleurisy may be palpable.

On *percussion over the affected lobe* (most frequently the lower right) the note, in the initial stage, may be slightly higher pitched and somewhat tympanitic (Skoda's resonance). When consolidation has taken place, the note is dull, but not absolutely flat, retaining usually a slight tympanitic quality. On resolution, the note gradually grows less dull, but it remains higher pitched than normal, and slightly tympanitic, for a long time (weeks or months) after convalescence has begun. In central pneumonia, outspoken dullness may be absent for days after the onset of the disease. When the lower lobe is involved, the percussion-note over the upper front of the chest is often lowered in pitch and sometimes slightly tympanitic, due to relaxation of the air-containing lung.

On *auscultation,* during the first twenty-four hours, that is, during beginning infiltration, fine crepitation is audible on inspiration (*crepitatio indux*). During the stage of consolidation, this fine crepitation disappears and loud bronchial breathing and bronchophony become audible over the dull area. Râles may be absent at this stage; if present, owing to a marked bronchitis, they are consonating. During resolution, the bronchial breathing gradually disappears, fine crepitation (*crepitatio redux*) reappears, and, later, coarser sounds (moist râles) become audible, especially on expiration; should the fine crepitation persist long, it is a sign of delayed resolution. Pleuritic friction is often audible. If the bronchus to the diseased lobe become plugged, the bronchophony and the increased vocal fremitus, otherwise present, may not be observable. It should be borne in mind that in the earlier stage of lobar pneumonia the breath sounds may be suppressed.

The *sputum* is scanty, very tenacious, and is often, though not always, of a rusty tint; many lancet-shaped diplococci and red blood corpuscles are present. Sometimes, small fibrin casts are visible. On resolution, the sputum becomes purulent, and later mucoid.

On *röntgenoscopy* one sees a clear lung field for several hours after the initial chill; then an even shadow appears over, as a rule, one whole lobe, growing gradually darker as hepatization proceeds; during resolution, the shadow grows less intense, but some shadow remains for from two to eight weeks after the attack.

The *fever,* at onset, rises rapidly to its height (103°-105° F.), and remains very constant during the fastigium or stadium acmes. The maximal temperatures are seen between the fourth and the sixth days. During the fastigium, the fever is, as a rule, slightly remittent, but it may be continuous, or, in rare cases, intermittent. The fever commonly ends by *crisis* (5th to 11th day), with sweats and slowing of the pulse and respiration; sometimes, a pseudocrisis precedes, by a day or two, the real crisis. Or, the fever may terminate by *lysis.*

The rate of the *pulse* is ordinarily from 100 to 116; in cases in which the pulse rises above 120, the mortality is high. Dilatation of the right heart sometimes occurs. The excretion of *chlorids* in the urine is suppressed. *Herpes labialis,* a frequent accompaniment, appears on the second or third day of the disease. There is nearly always a *leukocytosis* of from 12,000 to 60,000 or more; in the differential count the increase is seen to be in the polymorphonuclear neutrophils. In very grave infections, there may be a leukopenia instead of a leukocytosis. The *fibrin-content* of the blood and the *blood platelets* are increased. In many cases, a *blood culture* will reveal the presence of the pneumococcus.

In children, the initial chill may be replaced by a *convulsion.* The symptoms may simulate meningitis (delirium, vomiting, rigidity); while a true meningitis may complicate the disease, these symptoms are usually

due to intoxication (*meningismus*). Similar grave nervous symptoms may also be met with in adults. Drunkards may develop delirium tremens in pneumonia.

The *spleen* is probably always a little enlarged, but it becomes palpable in less than a quarter of the cases.

Vomiting is common in children at the onset; it is sometimes present

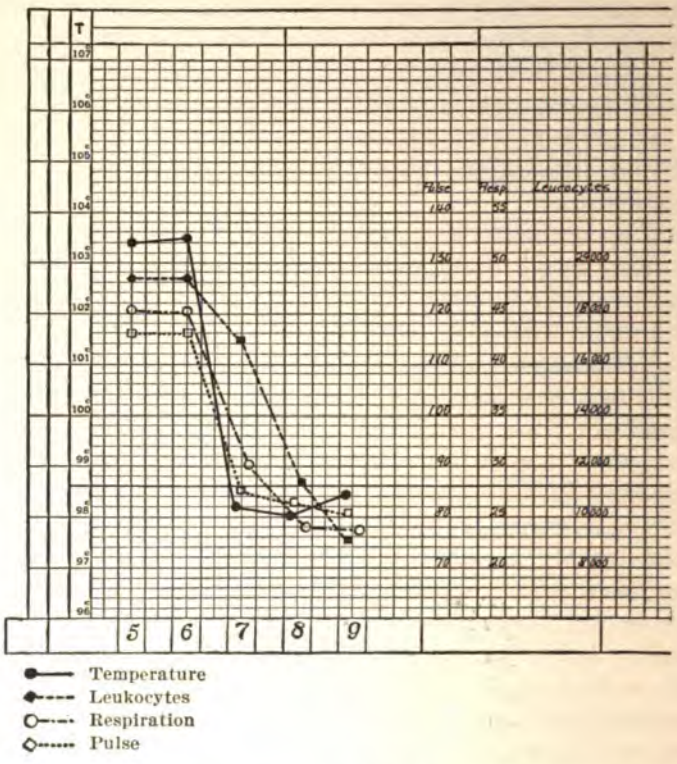

Fig. 169.—Pneumonic Crisis. Diagrammatic Chart Representing Relation of Temperature, Pulse, Respiration, and Leukocytes at Temperature Crisis in a Large Number of Cases of Acute Lobar Pneumonia. There is Also a Group of Cases in Which the Leukocytes and Respirations Come Down to Normal More Rapidly and Synchronously with the Temperature Crisis. (Compiled by Messrs. Tredway, Vanorden, Weinberg and Whitcraft; Med. Clinic, J. H. H.)

in adults, especially in apical pneumonia. In asthenic pneumonia gastro-intestinal symptoms (diarrhea, vomiting, slight icterus) may be marked.

Special Forms of Lobar Pneumonia.—When the upper lobe is involved (APICAL PNEUMONIA) the mortality is high. One lobe after another may become affected (wandering pneumonia or PNEUMONIA MIGRANS). Pneumonia is an especially fatal disease in drunkards (delirium tremens, heart failure, gangrene), in the aged, in the very young, and in patients suffering

from obesity, emphysema, or cardiac disease. Pneumonia involving both lungs is known as DOUBLE PNEUMONIA.

In CENTRAL PNEUMONIA, the physical signs usually present on percussion and on auscultation may be absent; there may even be no rusty sputum. The diagnosis has to be made as a probability diagnosis from the mode of onset, the febrile course, the tachypnea and the leukocytosis; in some cases, a positive blood culture (pneumococcus), or a central shadow on röntgenoscopy will be decisive.

In ASTHENIC PNEUMONIA, the course may be nearly afebrile and the physical signs atypical; the nervous and gastro-intestinal symptoms are often pronounced; the patients are markedly prostrated from the beginning, and may show the signs of what is often called a "typhoid state"; the course is often protracted and the mortality very high.

In so-called MASSIVE PNEUMONIA, there is dullness on percussion extending over the whole of one side of the thorax, accompanied by a feeling of great resistance on percussion. The bronchi are plugged with exudate and no sounds may be audible on auscultation. It is but little wonder that in such cases of massive pneumonia the condition is sometimes mistaken for a huge pleural effusion; but the heart is not displaced and Grocco's triangle of dullness is not present.

Complications.—These include empyema, pericarditis, endocarditis, meningitis; more rarely arthritis, nephritis or peritonitis. Abdominal pain is not uncommon at the onset of pneumonia; an acute surgical condition in the abdomen has often been suspected and exploratory laparotomy done!

Sequelae.—Abnormal terminations of lobar pneumonia include abscess of the lung, gangrene, tuberculosis, and chronic pneumonia (unresolved and organizing exudate).

Diagnosis.—In frank cases of lobar pneumonia little difficulty in diagnosis is experienced; the sudden onset with chill, fever, pain in the side, rapid breathing, cough, rusty sputum, and herpes, combined with the physical signs above described, is conclusive. Some difficulty may be experienced in the early stage of the disease in cases in which the subjective symptoms are masked by the presence of complicating conditions. Thus in cases of meningitis, of delirium tremens, in surgical accident cases, etc., the presence of a lobar pneumonia can readily be overlooked unless the investigation of the case and the analysis of the findings be thorough. At times the symptoms at onset may suggest other conditions; thus abdominal pain, vomiting, distention and frequently jaundice may lead to suspicion of the existence of peritonitis; or meningitis may be diagnosed because of the delirium, headache, fever and leukocytosis.

The slow development of the physical signs of consolidation often leads to confusion. The whole condition may erroneously be thought to be due to a simple pleurisy; or the slight impairment of resonance and the diminution in breath sounds that are found may be considered

insufficient evidence of pulmonary involvement. A röntgenogram of the chest may be of value, in obscure cases, at this time, for central pneumonias, or an early lobar consolidation may thus be clearly demonstrable.

The atypical physical signs observed over a massive pneumonia (absence of tubular breathing and vocal fremitus due to plugging of bronchi) have frequently led to confusion with pleurisy with effusion, or with an empyema. Should doubt exist, it is always wise to explore the chest thoroughly with a needle. Acute lobar pneumonia, especially when situated at one apex, may readily be confused with acute tuberculous bronchopneumonia. The further course will differentiate between these conditions readily but an early diagnosis often requires great skill in the interpretation of the data (history; physical signs; röntgenogram; sputum examinations including cultures; blood culture; leukocyte count, including a differential count). Caseous pneumonia involving a whole lobe and the pseudolobar form of bronchopneumonia are two conditions often mistaken for true lobar pneumonia of pneumococcal origin.

On entering a sick-room in winter when pneumonia is prevalent, an increase in the patient's respirations per minute may at once call attention to the possibility of a pulmonary involvement. I have been surprised to find how common it is for students and even for physicians of considerable experience to neglect this simple observation and to fail to think of the possibility of the developing pneumonia to which a tachypnea frequently points.

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NOTE.—For other references on Pneumonia see under Pneumococcus in Part IV.

(*b*) *Bronchopneumonia*

(Catarrhal Pneumonia, Lobular Pneumonia, Focal Pneumonia)

Definition.—This is usually an extension of a bronchitis to the lobules of the lung supplied by the single bronchioles—hence the term lobular pneumonia. A lobar infiltration may be simulated by the confluence of numerous bronchopneumonic foci. But focal pneumonia is not always secondary to a bronchiolitis; sometimes the bronchioles and the parenchyma

of the lung are simultaneously involved; or bacteria may be aspirated directly into the alveoli, causing a pneumonia not preceded by a bronchitis; sometimes, the focal process arises because of bacteria arriving by way of the blood vessels (see Embolic Pneumonia) or by way of the lymph channels.

Occurrence.—The disease is most common in childhood, frequently following measles, whooping-cough and influenza. Recurring attacks are often seen in children suffering from infected tonsils and adenoids. Many of the cases designated capillary bronchitis are really instances of bronchopneumonia with numerous small foci scattered through both lungs. Bronchopneumonia is not uncommon in the aged and enfeebled; it may occur also after operations ("ether pneumonia"), in some comatose patients (apoplexy, uremia), and in patients that vomit much (carcinoma ventriculi, peritonitis).

Etiology.—The infection is usually due to the pneumococcus, the streptococcus, Friedländer's bacillus, or the staphylococcus; occasionally, it is due to the Bacillus influenzae, the Bacillus coli, the meningococcus, the Bacillus pestis, the Micrococcus catarrhalis, or other bacteria. The bronchopneumonia is usually secondary to a preceding bronchitis of a descending type.

One form of bronchopneumonia, known as ASPIRATION PNEUMONIA or FOREIGN-BODY PNEUMONIA, follows the aspiration of food or other particles into the trachea and bronchi; it involves, usually, the lower lobes and is especially prone to become purulent or putrid.

In HYPOSTATIC PNEUMONIA, occurring in bed-ridden patients with faulty circulation, there is usually a slight bronchopneumonia with atelectasis. Indeed, in most bronchopneumonias, there are usually signs of more or less widespread atelectasis accompanying the focal infiltrative process.

Symptoms.—The clinical picture is far more variable than that seen in genuine lobar pneumonia. The patients show remittent fever, tachypnea, dyspnea, tachycardia and cyanosis. As a rule, both lungs are involved. When the foci of infiltration are close together, the diseased portion of the lung being as large as a silver dollar, a dull or slightly tympanitic note may be demonstrable; only rarely is there outspoken dullness.

On auscultation, numerous small and medium-sized rales, often consonating, can be made out over circumscribed areas, first, as a rule, over the lower lobes. Over larger infiltrations, bronchial breathing, bronchophony and increased vocal fremitus may become demonstrable. In influenzal pneumonia, many foci may appear simultaneously or successively, the physical signs (rales, roughened breathing, bronchophony) being very different over different foci; the foci of infiltration may, later, coalesce and cause consolidation of a whole lobe (*pseudolobar pneumonia*). Sometimes a "jumping" of the inflammatory process from one spot to another is

a striking feature, the bronchial breathing and crepitant râles soon disappearing from one spot and becoming audible at another.

The *sputum*, absent in young children, is in adults mucopurulent, and occasionally blood-stained. Cultures made on blood-agar, by Luetscher's method, from a washed ball of fresh sputum, will usually reveal the causal microörganism in pure, or in nearly pure, culture. Blood-agar is essential for the demonstration of the presence of hemoglobinophil bacteria like the *Bacillus influenzae*. The *fever* is more irregular than in lobar pneumonia; it often lasts three weeks or longer, and it ends by lysis.

There is always danger of circulatory failure either from failure of vasomotor tone or from weakening of the right heart owing to the obstruction in the pulmonary circulation.

Pleuritis, pericarditis, and otitis media are common complications. Tuberculosis often follows in persons predisposed to the disease. Abscess and gangrene of the lung occasionally occur as complications, especially in aspiration pneumonia. Severe diarrhea sometimes sets in, probably a toxic symptom. In the old, in the feeble, and in rachitic children, the outlook is grave.

Differential Diagnosis.—We must distinguish bronchopneumonia (1) from *atelectasis* (enfeebled breath sounds, absence of consonating râles, sometimes sudden disappearance of dullness after deep inspirations); (2) from *genuine lobar pneumonia* (onset, duration, crisis, and quick resolution); (3) from *pleuritis duplex* (exploratory puncture when in doubt); (4) from *pulmonary tuberculosis*, with or without complicating pyogenic infection.

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(*c*) *Metastatic* (*Embolic*) *Pneumonia*

This is always a part of some septic process, usually a phlebitis, somewhere in the body. Septic emboli, arriving through the pulmonary artery, cause septic infarcts, which may lead to embolic pneumonia, to lung abscess, or to gangrene. The pleura is often involved, and empyema or pneumothorax may follow.

The diagnosis rests upon the local signs combined with the demonstration of the existence of the primary infectious process elsewhere in the body.

(*d*) *Abscess of the Lung*

Definition.—A suppurative inflammation involving the lung substance.

Etiology.—In the *acute* and *subacute forms*, the pyogenic infection (1) may follow trauma, with tear of the lung; (2) may be due to septic emboli (in puerperal fever, thrombosis of cerebral sinuses, ulcerative endocarditis, phlebitis, etc.); (3) may result from rupture of an abscess into the lung (from the liver, subphrenic area, or retroperitoneum); (4) may follow aspiration of a foreign body; (5) may be a sequel to genuine lobar pneumonia, or to an influenzal or other form of bronchopneumonia; (6) may occur as a secondary process in cancer of the esophagus, tuberculosis, actinomycosis, or glanders.

In the so-called *chronic abscess* of the lung, we have to deal, as Fränkel has shown, less with actual abscess formation (in which a cavity arises from purulent softening) than with a necrosis followed by ulceration, the condition occurring in the course of subacute indurative pneumonia or in cirrhosis of the lung where necrosis may result from insufficient blood supply in the indurated tissue. Such a process should scarcely be designated "chronic abscess"; it would seem preferable to use the terms suggested by Charcot, namely "chronic ulcerative pneumonia" or "chronic ulcer of the lung."

Symptoms.—When abscess occurs as a sequel of lobar pneumonia, there is (1) delayed resolution of the pneumonic exudate, and (2) a continuance of the fever with the development of a "choppy" temperature chart due to morning remissions and evening exacerbations of the fever—always strongly suggestive, after pneumonia, of either empyema or lung abscess. At first the sputum may be of a greenish color, as in most cases of delayed resolution. Should the abscess rupture into one of the larger bronchi, the sputum becomes more abundant and is often coughed up in mouthfuls. This sputum is usually devoid of odor and is yellowish or brownish-yellow in color; on standing, the pus sinks in the form of a homogeneous yellow sediment, the supernatant fluid being gray and turbid. Sometimes particles or fragments of pigmented lung tissue are visible to the nal
As the abscess empties itself, the temperature may fall, and the al
signs of a cavity become demonstrable. Cavernous breathing

over the circumscribed area, the breath sounds often having an amphoric or a metallic character. Coarse bubbling râles may be heard, and sometimes metallic râles. A stereoscopic röntgenogram will reveal the exact size and position of such a cavity. In favorable cases, the inflammatory process gradually subsides, the signs of a cavity grow less distinct, the sputum diminishes in amount and becomes mucopurulent. As cicatrization proceeds, retraction of the chest wall may gradually develop.

The patients usually recover. In rare cases, gangrene of the lung may complicate the process; sometimes, an abscess of the lung ruptures into the pleural cavity and causes empyema; still more rarely, abscess of the lung may be followed by a general septicemia or pyemia.

Differential Diagnosis.—We must distinguish abscess of the lung (1) from perforated interlobar empyema; (2) from bronchiectasis; and (3) from pulmonary tuberculosis with cavity formation. We may derive much help from röntgenography and from bronchoscopy in cases difficult of diagnosis.

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(*e*) *Gangrene of the Lung*

(*Pulmonary Gangrene*)

Definition.—A condition in which a portion of the lung undergoes necrosis and putrid softening, the production of the foul-smelling substances being due to the presence of certain anaërobic bacilli. Gangrene may affect a solitary area, or it may, especially in chronic cases, involve several areas (multiple gangrene).

Etiology.—Pulmonary gangrene may have (1) a *vascular origin* due to septic and putrid emboli from gangrenous processes elsewhere in the body; (2) a *bronchial origin* as in the instances in which it follows putrid bronchitis and bronchiectasis, the aspiration of a foreign body (from the mouth, from an esophageal lesion, or, a lymph gland perforating a bronchus); or (3) a *pulmonary origin* owing to the presence of some destructive lesion in the lung (acute abscess, chronic ulcerative pneumonia, pulmonary tuberculosis, trauma). It is most often secondary to bronchiectasis and putrid bronchitis, but it occurs not infrequently also after influenzal pneumonia, aspiration pneumonia, and in carcinoma of the esophagus.

Symptoms.—As in putrid bronchitis, the sputum is inexpressibly foul and contains Dittrich's plugs. But in gangrene, particles or fragments of lung tissue are also present in the sputum, at least at times; in acute gangrene, large fragments may appear, whereas in chronic gangrene coarser fragments may be entirely absent over a period of months. Elastic fibers may or may not be present; they tend to disappear owing to the presence of a trypsinlike ferment.

There is some fever; the face looks pale and emaciated.

When a cavity has formed, there is paroxysmal coughing with mouthful expectoration, as in bronchiectasis; the patient instinctively assumes the posture in which the coughing spells are least frequent.

On physical examination, the findings depend upon the size of the cavity and its proximity to the surface of the lung. One may find a tympanitic area (surrounded by an area of dullness), exhibiting Wintrich's change of pitch on opening and closing the mouth; over the same area, amphoric breathing may be audible. The exact size and position of the cavity and the surrounding infiltration are most accurately determined by stereoscopic röntgenography; in a case of chronic gangrene that I saw with Dr. Holtzapple of York, Pa., the dimensions and the precise situation of the diseased area were easily demonstrable by this method.

Diagnosis.—This is easy when large fragments of lung tissue are present in foul sputum, exceedingly difficult when they are absent. As Fränkel emphasizes, the presence of dullness over the lower lobes with loud bronchial breathing does not suffice for a diagnosis of gangrene, no matter how foul the sputum may be, for such findings are not uncommon in putrid bronchitis with concurrent chronic pneumonia; an associated tympany may be due to relaxation of lung tissue near the infiltrated areas. The presence of amphoric breathing, however, speaks in favor of gangrene and often gives the clew to the position of the gangrene cavity. It is important to remember that in chronic gangrene, fragments of lung tissue may not be discoverable in sputum, even when regularly examined for months. The x-ray may be very helpful in the localization of a process believed to be gangrenous.

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II. THE INTERSTITIAL PNEUMONIAS

Occasionally, in man, an acute interstitial pneumonia results from purulent pleuritis (*pleurogenous pneumonia*), not unlike the pleuropneumonia of cattle.

Chronic forms of interstitial pneumonia are met with in the *pneumonoconioses* (*q. v.*), and sometimes in *tuberculosis* (*q. v.*).

III. THE SPECIFIC INFLAMMATORY PNEUMOPATHIES

Under this heading are included (a) pulmonary tuberculosis, (b) syphilis of the lung, and (c) certain other processes such as actinomycosis, streptothricosis, glanders, blastomycosis, and aspergillosis.

(*a*) *Pulmonary Tuberculosis*

(*Phthisis pulmonum*)

Definition.—A chronic disease of the lungs and bronchi due to infection with the tubercle bacillus.

Historical.—The disease was known to the ancients, and there are easily recognizable descriptions of it in the works of Hippocrates. Sylvius in the seventeenth century thought the nodules (*tubercles*) were enlarged lymph glands. Baillie at the end of the eighteenth century discovered the miliary tubercle; he distinguished also between conglomerate tubercles and caseous pneumonia. Great advances in clinical and pathological knowledge of the disease were made by the French physicians (Bayle, Laennec, Broussais) early in the nineteenth century. Virchow (1847-1852) made careful studies of the histology of tubercle, and Villemin (1865-1868) by a series of brilliant experiments on animals, established the *transmissible and infectious character* of the disease, showed the especial susceptibility of guinea-pigs, and asserted that the disease was transmitted from man to man by a virus present in the sputum. Vil-

lemin's views were at first disputed, but were soon corroborated by many workers, and notably by Cohnheim and Salomonsen, who devised the method of demonstrating the presence of the virus in pathological materials by inoculation of the anterior chamber of the rabbit's eye. The common nature of the virus in pulmonary tuberculosis, joint tuberculosis, gland tuberculosis, etc., was next established.

In 1882, the proof of the bacterial nature of the virus was brought by Robert Koch; he discovered, stained, and grew the *Bacillus tuberculosis,* and reproduced the disease by inoculation of pure cultures. A simple differential stain for this "acid fast" bacillus, very important as a diagnostic aid, was devised by P. Ehrlich. Extracts of the bacilli, known as *tuberculin,* were made by Koch, and used both for diagnostic and therapeutic purposes. Soon thereafter began the great *campaign for the prevention and cure* of tuberculosis (dispensaries, sanatoria, national and international conferences).

Pathology.—Tuberculous inflammations of the lung occur in two forms: (1) *tuberculous granulation* (with tubercle formation), and (2) *caseous pneumonia.* The former is a productive, the latter an exudative inflammation. The former develops in the interstitial tissue; the latter fills the alveoli with exudate. Both are due to the same bacillus, and the two processes may go on together in the same lung. Formerly, one out of every six or eight deaths was due to tuberculosis; but in recent years the mortality rate from the disease has begun to decrease.

Of the *main types* of pulmonary tuberculosis may be mentioned:

1. ACUTE DISSEMINATED MILIARY TUBERCULOSIS (distribution of bacilli through the blood; usually part of a general miliary tuberculosis; where only one lung or one lobe is involved, the distribution may be bronchogenous from coughing).
2. CHRONIC PULMONARY TUBERCULOSIS (beginning usually in the apices, and gradually extending to the lower portions of the lungs and to the pleurae, healing with induration in some places, extending, or softening, in others).
3. ACUTE TUBERCULOUS PULMONARY PHTHISIS (like 2, with signs of rapid cavity formation, or with extensive caseous pneumonic processes, in the most rapid cases giving rise to *galloping consumption*).

Etiology.—Pulmonary tuberculosis is due to reactions of the lungs to infection with Koch's *Bacillus tuberculosis;* the disease is, however, often complicated by mixed infections with other bacteria (influenza bacilli, streptococci, pneumococci, etc.), these mixed infections accounting for much of the fever and cachexia, and, perhaps, for the amyloid degeneration of the organs that sometimes occurs. To understand how the disease develops (phthisiogenesis), it is necessary to study not only *mod tion,* but also the *conditions of disposition.* Tuberculous infe in everyone that lives to become an adult; the progressive leads to pulmonary phthisis develops in not over one-tenth o

Modes of Infection.—The bacilli reach the lung in various way by aspiration or aërogenous infection (droplet infection, laryngeal

tonsillar tuberculosis), sometimes by lymphogenous or hematogenous infection, through the lymph channels or the blood channels (secondary to tuberculous otitis, tuberculous enteritis, tuberculous adenitis, tuberculous pleuritis, etc.).

When the *Bacillus tuberculosis* was first discovered, it was thought that aspiration of the bacilli explained the source of human infection in nearly all cases. Later studies have led to the consideration of many other modes of infection.

Experimental studies on animals have been extensively made, and the effects of intravenous, subcutaneous, intra-ocular, and intraperitoneal inoculation, as well as of feeding experiments and inhalation experiments, have been carefully watched. And, in general, it may be said that, aside from direct inoculation into the blood stream, there is always first, no matter what the portal of entry, an involvement of the regional lymph glands, this involvement of the lymphatic apparatus often occurring without signs of pathological change at the actual portal of entry.

Studies of tuberculous human beings indicate that human infection does, in reality, occur in several different ways. CONGENITAL INFECTION is rare, but has been indisputably proven to take place; it is not a germinal infection, but comes always from the mother through placental tuberculosis. INTESTINAL INFECTION, as primary, has recently, through the studies of Behring, of Heller, and of Councilman, Mallory and Pearce, assumed considerable importance. In children, previously apparently healthy, dying of diphtheria, about 6 per cent are found to show signs of primary intestinal tuberculosis (in the mesenteric lymph glands). About half the cases of primary infection through the intestine are due to the bovine type of bacillus, the other half to the human type. TONSILLAR AND MOUTH INFECTION, as shown by tuberculosis of the cervical lymph glands, is very common in childhood; how often it leads to pulmonary tuberculosis is not known; when it does so, the bacilli reach the lungs in all probability by passing from the cervical glands to the lung, neither by way of the bronchial glands nor by way of the lymphatics to the pleura, but rather by entrance, first, into the venous system and thence through the right heart to the lungs. INHALATION INFECTION OR AËROGENOUS INFECTION is held by many to be the commonest mode of contracting pulmonary tuberculosis. The evidence is strongly in favor of this view for chronic pulmonary tuberculosis beginning in the apices, the apices being especially predisposed on account of (1) the minimal energy of the movement of the air during expiration there, and the corresponding lessened energy of the lymph current in the same situation (Tendeloo), and (2) the predisposing influence of stenosis of the upper aperture of the thorax in persons of the habitus phthisicus due to congenital shortening and ossification of the cartilage of the first rib (W. A. Freund), this peculiarity of the first rib giving rise to a groove-like constriction of the apex of the lung (Schmorl) and to a faulty development of the bronchial tree at the apex (Birch-Hirschfeld), conditions that, when experimentally simulated, predispose strongly to both aërogenous and hematogenous tuberculous infection of the apices in animals (Baemeister). Acute pulmonary tuberculosis (acute or galloping consumption) arises, however, in a different way; thus in the *lobar* or *pseudolobar caseous pneumonia*, the cause is most often found to be the aspiration of large numbers of tubercle bacilli either from a tuberculous lymph gland perforating into a bronchus, or from a tuberculous cavity due to a preëxisting chronic tuberculosis, and in the *disseminated form of acute tuberculosis* the miliary tubercles may arise either through a bronchogenous distribution of the bacilli (through coughing or through aspiration) or through a hematogenous distribution (through rupture of a caseating focus into one pulmonary artery).

The tubercle bacilli have their source chiefly in tuberculous human beings, partly in tuberculous animals (cows). Infected human beings may give off

bacilli in various ways; by far the most important discharge is tuberculous sputum, though urine, feces, pus, discharge from lupus, etc., may occasionally be responsible. The bacilli of sputum may reach other persons by direct contact (fingers, kissing), by the spray produced by coughing (droplet infection of Flügge), and by dust containing dried sputum (careless expectoration), especially in dwelling-houses, hotels, theaters, factories, and shops, since street-dust seems rarely to be responsible.

Uncooked milk, cream, and butter may spread the bovine type of the bacillus; meat is less often responsible. About half the cases of tuberculosis of the intestine and the mesenteric glands are due to the bovine type; it is rare, however, to find the bovine type in human pulmonary tuberculosis.

Conditions of Disposition.—Most people—probably all—that live to be thirty years of age become *infected* with the tubercle bacillus. Fortunately, the *infection* does not cause *sickness* in the majority. As has often been emphasized, every infectious disease is the product of infection and disposition. In order that the disease occur, the relations of infection and disposition must be such "that the sum of both is larger than in patients that do not sicken" (Staehelin). There appears to be a local *disposition* to pulmonary phthisis as well as a constitutional predisposition to tuberculous infection; all men have some of the latter, but the former is often a family affair. Thus, one predisposed to pulmonary phthisis may have a long narrow thorax (thorax phthisicus) with short and early-ossified first-rib cartilage (see above), hypoplasia of the heart and of the aorta, and visceroptosis (habitus asthenicus). Besides the hereditary local predisposition, there are other accidental predisposing factors: namely (1) certain infectious diseases (measles, whooping-cough, influenza); (2) the pneumonoconioses (anthracosis, siderosis, chalicosis, etc.); (3) prolonged physical or mental over-exertion; (4) prolonged under-nutrition and life under non-hygienic conditions; (5) diabetes; and (6) pregnancy. On the other hand, pulmonary tuberculosis is rare in persons that suffer from emphysema or from chronic heart disease. On the side of *exposure*, frequent contact with infected persons, leading to multiple reinfections, is undoubtedly of great importance in the development of the disease.

When tuberculosis is suspected, therefore, the anamnesis should be taken with especial care. One should gather data on the following points:

1. Is there any history of tuberculosis, pleurisy, scrofula, meningitis, or hip-joint disease in the family (parents, sibs, husband or wife, children), or has the patient lived in a house or worked in a shop with infected persons?

2. Has the patient himself previously suffered from hemoptysis, pleurisy, hoarseness, cough or enlarged glands?

3. Has the patient been exposed to great hardship or overwo
woman, to many pregnancies or to prolonged lactation?

4. Does the occupation of the patient predispose (exposure to d
cold; alcoholism, etc.)?

5. Has the patient recently lost weight or suffered from cough,
or with unexplained digestive disturbances?

Clinical Examination.—Tuberculous patients often present

istic appearance, the so-called phthisical constitution (*habitus phthisicus*). They may look pale, thin and feeble, have a delicate bony framework, with a long, narrow, flattened thorax with wide intercostal spaces (thorax paralyticus, expiratory type of thorax). The pulse and the respiration are often accelerated. There may be intermittent fever (*febris hectica*), with tendency to night sweats. The hair may look unhealthy, the sclerae bluish, and there is often a skin infection, pityriasis versicolor. Search should always be made for signs of previous scrofula or of infantile tuberculosis (scars in the neck, corneal opacity, bone and joint lesions).

i. Ordinary Chronic Forms of Pulmonary Tuberculosis

For convenience, it is customary to distinguish three stages or degrees of the ordinary form of pulmonary tuberculosis.

Stage 1.—Initial, incipient or developmental period (*phthisis incipiens*).

Stage 2.—Stage of well established infiltration (*phthisis confirmata*).

Stage 3.—Terminal stage, with signs of cavity formation (*phthisis consummata, stadium colliquationis*).

In referring patients to sanitaria or to other physicians for treatment, it is customary to speak of three grades, or classes, of patients.

1. *Mild cases*, in which the disease is limited to a small area in one lobe, especially at one apex, but not extending below the clavicle or the spine of the scapula, and with or without fine râles that are non-consonating.

2. *Cases of medium severity*, the disease extending beyond the limits of 1 but not as far as 3.

3. *Advanced cases* with involvement of one whole lobe or of several lobes, or with signs of cavity formation.

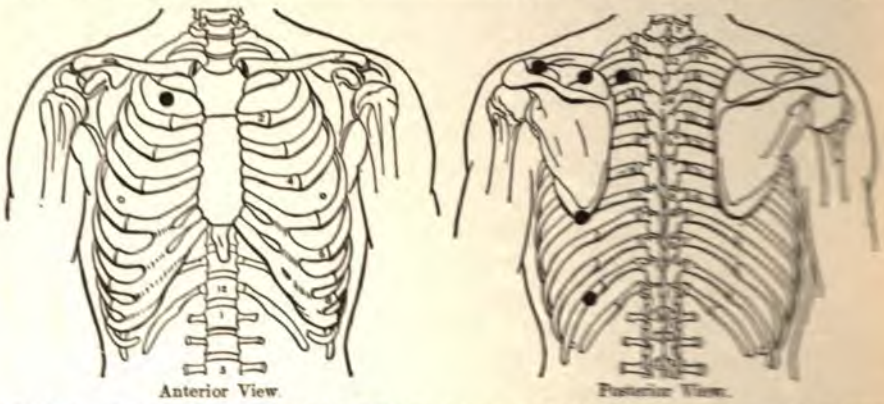
Epitome of the Physical Signs.—**Stage 1** (*Phthisis incipiens, Apical Catarrh*).—Râles are usually audible at one apex in front or behind; these may be either fine crepitant râles or rhonchi. The respiratory murmur is either enfeebled or roughened, with prolongation of the expiratory sound, cog-wheel breathing or indefinite breathing. The percussion note may be normal, or only slightly shorter and a little higher pitched than normal; usually there is demonstrable narrowing of the area of apical resonance. Occasionally, a slight lagging of the movement of the affected side can be made out on inspection. Dry cough is a common symptom, especially in the early morning, with scanty sputum or none; tubercle bacilli are occasionally demonstrable in the sputum, but by no means always. Hemoptysis is not uncommon.

The student should remember that *a chronic catarrh of one apex is most often tuberculous in nature.* This is an extremely common disease, though in the majority of instances it heals, leading only relatively rarely to a progressive phthisis.

Several varieties of phthisis incipiens have been distinguished. Thus Staehelin includes (a) a *catarrhal form*, resembling at onset an ordinary

bronchitis after catching cold; (b) an *anemic form*, in which anemia, palpitation and tachycardia are striking symptoms; (c) a *dyspeptic form*, in which disturbances of digestion bring the patient to the physician; (d) a *febrile form*, in which an obscure fever may last for some time before the pulmonary origin becomes recognizable; (e) a *pleuritic form*, in which either a dry or a wet pleurisy is the first recognizable change; (f) a *hemoptoic form*, in which the first sign is the spitting of blood; and, finally, (g) a *traumatic form*, in which the signs of pulmonary tuberculosis develop a few weeks or months after a contusion of the chest.

Stage 2 (*Phthisis confirmata, Stage of Definite Infiltration*).—At this stage, the disease extends beyond the apex. The dullness in front, above the clavicle, is continuous with dullness as far down as the second or the third rib, and, behind, there is dullness in the fossa supraspinata; usually slightly tympanitic resonance can be made out in the corresponding upper



Anterior View. Posterior View.

Fig. 170.—Regions of the Thorax Over Which Percussion and Auscultation Should Be Carried Out Systematically in Suspected Tuberculosis

chest on light percussion. Over the dull area, even bronchial breathing, with dry and moist râles, often consonating, is audible. Whispered voice sounds are markedly increased in affected areas. When, on the right, râles are audible as low as the third intercostal space or the fourth rib, the middle lobe has become involved as well as the upper. There is diminished expansion, or lagging, on the affected side, often with signs of retraction of the upper lobe. As the disease extends gradually downward in the lung first affected, the apex of the other lung usually becomes involved. The sputum is more abundant than in the first stage, is purulent and usually contains tubercle bacilli. There may, or may not, be fever. Usually there is a gradual, sometimes a rapid, loss of body-weight. Hemoptysis is not uncommon.

This stage of pulmonary tuberculosis must be differentiated from (1) simple chronic bronchitis, (2) bronchiectasis, (3) the pneumonias, and (4) chronic non-tuberculous pneumonias.

Stage 3 (*Phthisis consummata, Advanced Tuberculosis with Cavity Formation*).—This last stage is characterized by widespread infiltration of both lungs, and, especially, by the formation of cavities. The extent of the infiltration can be determined by demonstration of the areas over which tympanitic dullness, bronchial breathing, increased fremitus, râles and bronchophony exist. Both lungs are involved; sometimes the lower lobes as well as the upper are infiltrated. Retraction of the upper lobes, due to fibroid change, causes contraction of the upper thorax with deepening of the supra- and infraclavicular fossae and of the upper intercostal spaces. Signs of cavity formation are usually present (bubbling râles, metallic tinkling, loud bronchial or amphoric breathing, cracked-pot resonance, change of pitch on percussion). The *sputum* is mucopurulent, free from air bubbles, often nummular or coin-shaped, and loaded with tubercle bacilli; sometimes it contains elastic fibers or blood.

In this terminal stage, the *fever* is often high, due to mixed infection with pyogenic cocci, but it may be subnormal. *Night sweats* are a troublesome symptom. The emaciation may become extreme.

The diagnostic tuberculin tests (von Pirquet, Calmette, etc.) and other points bearing upon diagnosis are described in the section on Infectious Diseases.

Acute Form of Pulmonary Tuberculosis

(*Phthisis florida, Galloping Consumption*)

Under this heading we include (a) the pneumonic form, and (b) the multiple focal form.

(a) Pneumonic Form, Including Caseous Pneumonia.—In the peracute cases, the onset may resemble that of ordinary lobar pneumonia, except that there is rarely any chill, the fever is less regular and the sputum not rusty. Death may occur within two weeks (primary alveolar pulmonary tuberculosis of Heller and Hedinger).

In less acute cases, the onset may be similar, suggesting croupous pneumonia, but the course is somewhat less rapid than in the peracute cases above described. The sputum may be gelatinous, greenish, though sometimes it is rusty. Tubercle bacilli may be present at first, though as a rule they are not found until later. Pneumococci may be present in considerable numbers and help to mislead the diagnostician. An early and intense diazo-reaction in the urine speaks for caseous pneumonia rather than for ordinary lobar pneumonia. The practitioner may first have his eyes opened by the failure of a crisis to appear and the persistence of the infiltration beyond the ordinary period of lobar pneumonia. Coarse râles develop and a little later perhaps typical cavernous symptoms. The sputum becomes nummular; the fever becomes irregular; and the patient goes rapidly down hill. Death often occurs at the end of six weeks just as

cavities are beginning to form. Some patients linger on until large cavities form; in such instances, the disease may become temporarily arrested, and the patients regain some health and strength, but, as a rule, even then, cure does not occur, the patients dying ultimately with the signs of chronic cavernous pulmonary tuberculosis.

(b) Disseminated Forms of Acute Tuberculosis.—Galloping consumption, instead of taking the pneumonic form above described, may be due to the simultaneous development of multiple foci, usually involving both lungs. Three main types may be distinguished: (1) a *disseminated* [illegible] most often met with in diabetes and in chronic alcoholism; [illegible] in which the bacilli are distributed with the blood [illegible] occurring within a month after the hemorrhage; [illegible] *peribronchitic* or *nodular form*, due to aspiration of [illegible] small bronchi.

[illegible] in the one hand, have been apparently entirely [illegible] other hand, such an acute disseminated focal tuber[illegible] patients that have had a simple apical tuberculosis, [illegible] suffered for some time from ordinary chronic pul[illegible] Such acute outbreaks are most common in persons that [illegible] immunity to tuberculosis, either because they have not [illegible] infectious (doubtless responsible for the rela[illegible] adults), or because immunity has in some way been [illegible] influenza, pregnancy, lactation, alcoholism).

[illegible] especially difficult in the acute peribronchitic [illegible] healthy before. The condition is often [illegible] persistent influenza, as typhoid fever, or as acute [illegible] to rely upon most careful physical exami[illegible] bacteriological studies of the sputum and [illegible] Widal, Calmette), the presence or absence of [illegible] other than the lungs (meninges, choroid, intes[illegible] [illegible] studies.

[illegible] diagnosis soon becomes clear, and in the [illegible] difficulty.

[illegible] Pulmonary Tuberculosis.—Among the complications [illegible] mentioned pleuritis, laryngeal tubercu[illegible] tuberculosis, and general miliary [illegible] occasionally occurs. In advanced [illegible] of the organs (splenomegaly, [illegible] is often made worse by pregnancy. [illegible] tuberculosis are prone to lower [illegible] pertussis).

[illegible] death may occur from asphyxia[illegible] from hemorrhage (hemoptysis), or from [illegible] (propneumothorax); occasionally, it

results from cardiac failure (chronic intoxication, pulmonary obstruction). In a few cases, death is due to general miliary tuberculosis or to general amyloid degeneration. Not infrequently, in advanced stages, death is due to an intercurrent infection (lobar pneumonia, influenza, streptococcus sepsis).

Röntgenography and Röntgenoscopy in Pulmonary Tuberculosis.—Examinations by means of Röntgen rays are less important for the diagnosis of the existence of pulmonary tuberculosis than for the recognition of the extent of the disease and the distribution of the pathological foci in the

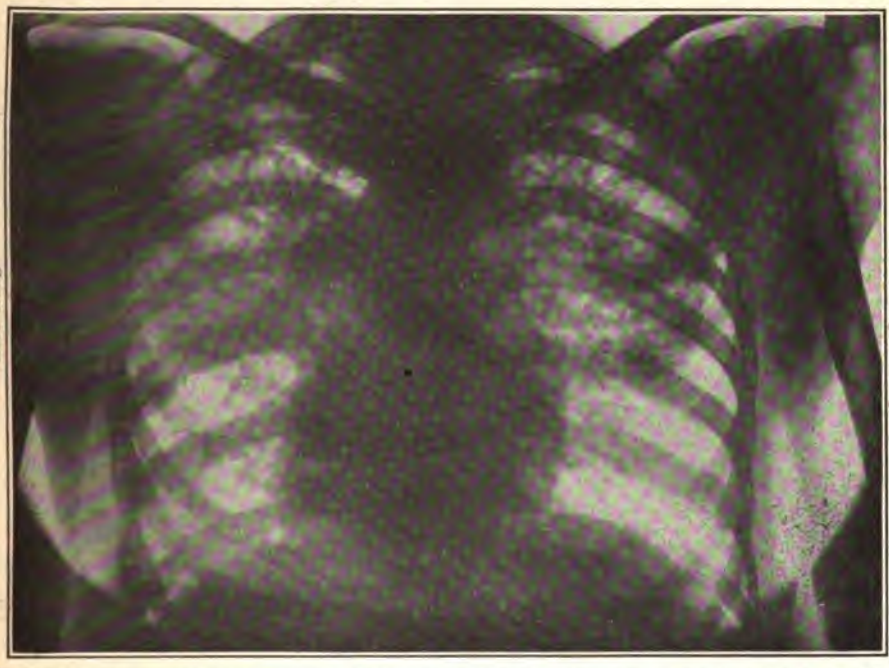


Fig. 171.—Pulmonary Tuberculosis. Extensive Infiltration Found in a Medical Student, Who Had Worked Up to a Few Days Before, Unaware of Infection. (X-ray Dept., J. H. H.)

lungs. In x-ray plates of the lungs, infiltrations throw a shadow, whereas cavities appear as clear areas.

The shadows due to infiltration are not evenly diffuse, but are mottled. Some experience is necessary in interpreting the x-ray plates, since normally the hilus of the lung and the bronchial tree cause some mottling. Mere enlargement or increased intensity of the hilus shadows, even with strandlike shadows radiating toward the apices, are to be very cautiously interpreted. The meaning of the hilus shadows is only gradually being worked out. Changes in these hilus shadows are undoubtedly sometimes due to tuberculosis, but they may also follow upon non-tuberculous processes (chronic lymphadenitis simplex, chronic passive congestion, chronic

bronchitis, etc.). When, however, the mottling is asymmetrical, or is seen in the periphery of the lung area, or extends downward from a diffuse shadow at one apex, it is to be regarded as very suspicious of tuberculosis. Röntgenoscopy alone is insufficient for the study of pulmonary tuberculosis, though it is often very helpful for a general preliminary orientation. Röntgenography is, as a rule, necessary, and soft tubes yielding good contrasts should be used. It is best to take (1) a view of the whole chest on a large plate (30 × 40 or 40 × 50 cm.) at a focal distance of 50-60 cm., the

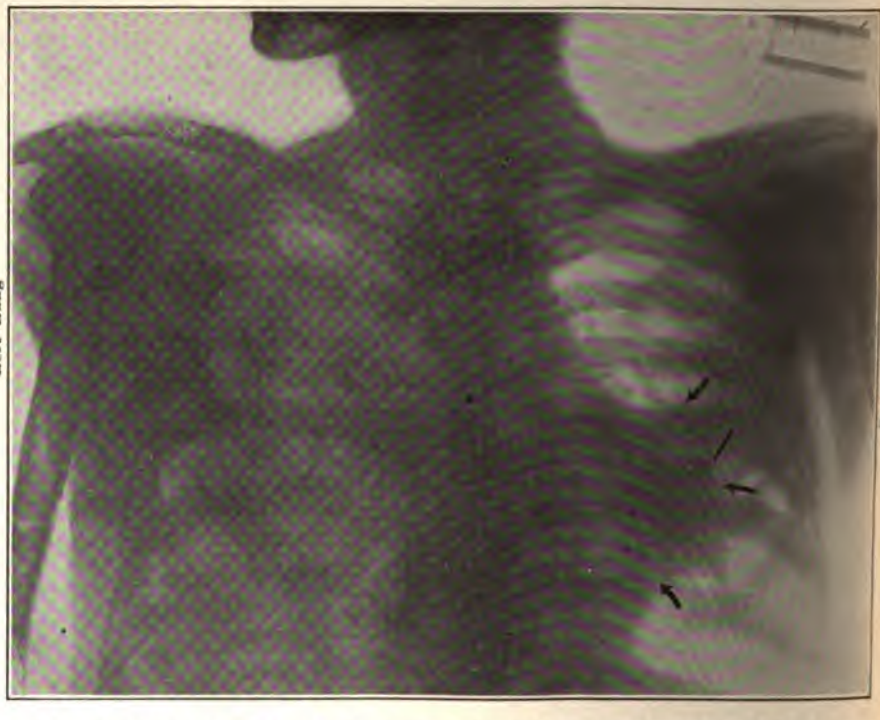


Fig. 172.—Tuberculosis: Thickened Pleura on Left; Cavity on Right, Which Was Obscured by Thickened Pleura, as Was Shown at the Post Mortem; Adhesions on Right Side. The Arrows Indicate Pleural Thickening on the Right Side Over a Cavity. (X-ray Dept., J. H. H.)

rays being passed through in the dorsoventral direction, so as to avoid too much bone shadow, and (2) a partial view of an apex down to the hilus on a smaller plate (24 × 30 cm.), using a tube or diaphragm and a focal distance of 40 cm. Stereoscopic plates are especially helpful.

Pleural thickenings may be recognizable as diffuse shadows. Adhesions to the diaphragm may give rise to projections or puckerings of the upper surface of the diaphragm as seen in the x-ray plate. Calcification of the cartilage of the first rib should always be looked for. Often intense circumscribed shadows will be found near the hilus or toward one apex;

they usually indicate calcified lymph glands or lime deposits in healed foci of tuberculosis in the lung.

A *cavity* appears in an x-ray plate as a clear, round area, surrounded by a ringlike shadow. The latter is well brought out if the exposure be made through a narrow diaphragm. Of course, if the cavity be filled with sputum, it will give rise to a shadow in the röntgenogram instead of to a clear area. Irregularities in the wall of a cavity, or subdivision of the cavity into several chambers, can occasionally be made out.

The *respiratory movements* are changed in pulmonary tuberculosis;

Fig. 173.—Generalized Tuberculosis of the Lungs. Arrows Show Cavity in Left Upper Lobe. (X-ray Dept., J. H. H.)

less air is taken into the diseased lung on inspiration and the diaphragm excursion is less (Williams' symptom); this phenomenon is often demonstrable by röntgenoscopy in incipient apical tuberculosis. This symptom is, however, less valuable for diagnosis than was formerly thought, since it is demonstrable in only a minority of the cases, and, moreover, may be present in cases of healed tuberculosis.

Valuable as x-ray examinations are in the study of pulmonary tuberculosis, it must be emphasized that there are often marked discrepancies

between x-ray findings and the general physical findings (F. H. Baetjer and L. Hamman). Either may help to a positive diagnosis when the other is almost negative. As a rule, however, the x-ray examination reveals in positive cases, a wider distribution of the tuberculous process than would be suspected from the examination by percussion and auscultation.

In the *third stage* of pulmonary tuberculosis, with extensive infiltration and cavities, the x-ray plate gives a better idea of the extent of the process than any other method of examination.

During the treatment of pulmonary tuberculosis by production of arti-

Fig. 174.—Artificial Pneumothorax. Arrows Indicate Collapsed Lung; Crosses Indicate Pneumothorax. (X-ray Dept., J. H. H.)

ficial pneumothorax (Forlanini), x-ray examinations offer an excellent method of control.

For other facts regarding pulmonary tuberculosis see Section on Infectious Diseases.

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(*b*) *Syphilis of the Lung*

(*Lues pulmonum*)

A rare condition in adults, met with sometimes in the tertiary stage (gummata). Besides the gummatous form, a chronic, sclerotic, interstitial pneumonia may be due to lues. It is rarely met with in the apices; gummata most often develop in the lower lobes or in the middle lobe on the right side. A dry cough with mucoid sputum and dyspnea are usually the first symptoms. A few râles over an area of circumscribed dullness may be discoverable, most often in the middle lobe on the right side.

Lung syphilis may closely simulate tuberculosis. Indeed, most cases syphilis are treated for a long time for tuberculosis before the true natu covered. The differential diagnosis is all the more difficult since (1) I tuberculosis may occur in luetic patients that have no syphilis of the

(2) pulmonary tuberculosis and pulmonary syphilis may coexist in the same patient!

Cavity formation is rare. There is no single, absolutely certain, criterion for diagnosis, and the disease may be confused not only with tuberculosis, but also with bronchiectasia, with abscess, with neoplasm, or with chronic pneumonia. A probable diagnosis can be made if the disease be thought of, if the Wassermann be positive, if the x-ray reveal a large hilus shadow with outrunners, if tubercle bacilli are permanently absent from the sputum, if there be but little fever, if the process involve especially the middle of the lung, and if there are signs of syphilis in other organs. If the symptoms and signs disappear under specific anti-luetic therapy, the diagnosis is confirmed, though it should be borne in mind that the sclerotic form of pulmonary syphilis will be but little influenced by therapy. In association with syphilis of the lung, the existence of laryngeal syphilis or of syphilis of the trachea or bronchi may be demonstrable. Amyloid degeneration of the organs may complicate the clinical picture.

I have seen one case in which a luetic infiltration widespread throughout one lung cleared up entirely under salvarsan therapy. Hereditary syphilis of the lung is not uncommon in the fetus and in the new-born. Most often it takes the form of an interstitial pneumonia; a catarrhal pneumonic form, known as pneumonia alba (Virchow), also occurs; in rare instances, one sees circumscribed gummata.

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(c) *Other Specific Inflammations of the Lung*

Actinomyces, glanders, blastomyces, and aspergillum may affect the lungs, but such infections are rare. (See Infectious Diseases.) Streptothricosis of the lung is occasionally met with; it may resemble pulmonary tuberculosis closely clinically.

Infiltrations of the lung also occasionally occur in leukemia, and in the several pseudoleukemias, including Hodgkin's disease.

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2. Pneumopathies Characterized by Alterations of the Alveolar Lumen

Under this heading we include (a) atelectasis, and (b) emphysema pulmonum.

(*a*) *Atelectasis*

Definition.—When the pulmonary alveoli are empty of air, and their opposite walls come into apposition, so as to resemble the fetal state of the lung, the condition of atelectasis or collapse exists.

Etiology.—Atelectasis, or apneumatosis, may be congenital or acquired. In CONGENITAL ATELECTASIS, areas of the lung substance fail to take in air and remain in their fetal state owing to insufficient expansion of the chest because of feeble muscles or faulty innervation. In ACQUIRED ATELECTASIS, lung that formerly contained air becomes devoid of air and the alveoli collapse and reassume a state similar to the fetal. ~ h acquired atelectasis may be due (1) to enfeeblement of the inspira muscles, (2) to compression of the lungs owing to encroachment upo intrathoracic space, or (3) to stenosis of the air-tubes.

In ATELECTASIS DUE TO FEEBLE CONTRACTION OF THE MUSCLES SPIRATION, or so-called "marantic atelectasis," the cause is to be sou some prostrating disease (*e. g.*, rickets, diarrhea, typhoid fever or s

Compression atelectasis may be due to accumulation of fluid or gas in the pleura or in the peritoneal sac, or to the growth of mediastinal tumors, aneurisms, or intrathoracic strumata, to such an extent that the pressure on the adjacent lung is equal to or greater than the inspiration pressure. Again, compression atelectasis may follow encroachment upon the intrathoracic space and interference with the contractions of the diaphragm from below, as by meteorism, ascites, or large abdominal tumor. The atelectasis seen in kyphoscoliosis is also a compression atelectasis.

Stenotic or obstructive atelectasis depends upon the complete plugging of a bronchus by inflammatory secretion, by an aspirated body, or by a tumor, with subsequent absorption of the air from the corresponding lobule of the lung. This form of collapse is commonest in the capillary bronchitis of children complicating measles, whooping-cough and other infections.

Symptoms.—In *atelectasis of the new-born,* the symptoms consist of dyspnea, cyanosis, distention of veins, retraction of the lower thorax during inspiration in the form of a deep furrow at the level of the 6th and 7th costal cartilages. Fever and cough may be absent. The pulse is slow, the right heart is labored and the pulmonic second sound accentuated. In severe cases, attacks of asphyxia may occur. Occasionally there is sinus thrombosis due to stasis; the child becomes drowsy and shows paresis of one side of the face and distention of the jugular veins of the same side. Prolonged bilateral atelectasis after birth may be the cause of a peculiar deformity of the thorax known as the wasp-waist (*Wespentaille*) of Francke, in which the anteroposterior diameter of the chest is increased above, and the lower thorax is separated from the upper by a groovelike constriction.

In *acquired atelectasis,* the condition is always an accompaniment of some other pathological process (see etiology), and the physician may experience much difficulty in deciding which of the signs are due to atelectasis and which to the primary process. Thus atelectasis is common in the periphery of a bronchopneumonic focus. Over atelectatic areas, say at the bases of the lungs, we find dullness and suppression af the breath sounds; after a forced inspiration, the dullness may lessen and the breath sounds become louder. At the upper margin of an atelectatic area, crepitant râles often become temporarily audible on inspiration deep enough to overcome the bronchial obstruction.

Diagnosis.—The main difficulty lies in distinguishing acquired atelectasis from a pneumonic process. When atelectasis and bronchopneumonia are simultaneously present, the diagnostic acumen of the most skilled is severely taxed. Fever is absent in uncomplicated atelectasis, but fever may be absent in pneumonia in a feeble child or in an aged person. The sudden lessening of dullness and the loudening of the breath sounds after deep inspirations are perhaps the most important criteria in the diagnosis

of atelectasis. As acquired atelectasis is a secondary phenomenon, it may sometimes be suspected from the character of the primary disease.

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(*b*) *Vesicular Emphysema of the Lungs*

(*Emphysema pulmonum*)

Definition.—A condition in which there is enlargement of the lungs with an increased air content. In ACTIVE LUNG DISTENTION (*simple lung distention, volumen pulmonum acutum*) there is an abnormal distention of the alveoli with temporary or permanent loss of elasticity; in many instances there is a return to normal when the cause is removed. It may be diffuse, involving both lungs as in bronchial asthma, or it may affect certain parts only; in the latter instance, it is usually a vicarious (or collateral) emphysema, due to interference with the function of other parts (through atelectasis, tuberculosis, pneumonia, or compression).

In CHRONIC, TRUE, OR SUBSTANTIAL, VESICULAR EMPHYSEMA the increased air content of the lungs is associated with an actual atrophy of the lung substance, neighboring alveoli or even large groups of alveoli fusing to form larger air cavities. The lungs become permanently dilated, their margins overlap the heart, and those of the two lungs may meet in front, obliterating the superficial cardiac dullness.

Etiology and Pathogenesis.—An acute lung distention is a common accompaniment of attacks of bronchial asthma, of acute capillary bronchitis, and of exacerbations of a chronic bronchitis.

Chronic vesicular emphysema seems to depend upon mechanical influences acting upon lungs of abnormally low resistance, especially of their elastic fibers. In most cases the emphysema is secondary to a chronic bronchitis. It is often met with in horn-blowers, glass-blowers, singers, public speakers, and men that do heavy lifting or much stair-climbing. That there may be a congenital weakness of the elastic tissue of the lungs in those affected is favored by the fact that "emphysematous families are known." Still, the main cause seems to lie in the bringing of the thorax, over a long period, into an exaggerated position, secondary to which a distention-atrophy of the alveolar walls develops (Tendeloo). Men are twice as often affected as women. Asthma, chronic bronchitis, and bronchiectasis are common accompaniments.

The thorax becomes barrel-shaped and immobile in the position of deep inspiration. The ribs and the sternum are displaced forward and upward, so that the anteroposterior diameter of the chest is increased. The intercostal spaces are widened; there is premature ossification of the rib carti-

lages. Freund believes that the emphysema is secondary, like the deformity of the thorax, to changes in the costal cartilages, but Fränkel opposes this view. Owing to the fact that many of the alveolar walls with their capillaries are destroyed, hypertrophy, and, later, dilatation of the right ventricle occur; ultimately, myocardial insufficiency develops and may be the cause of death.

Symptoms.—In pronounced cases, the barrel-shaped thorax (see above) is a characteristic feature. Slight grades of emphysema may cause no distressing symptoms except when complicated by bronchitis or asthma. In severer cases, chronic bronchitis is almost always present and is associated with dyspnea and cyanosis. The respiration, which is chiefly abdominal, is accelerated, and the expiratory character of the dyspnea is marked. The cyanosis may reach a high grade; it becomes more marked on muscular exertion, or during a complicating bronchitis, or when myocardial insufficiency sets in. The veins of the neck and head are usually distended, and there is often venous ectasis of the skin opposite the attachment of the diaphragm.

On *percussion* there is hyperresonance, the tone being louder and of lower pitch than normal (boxlike tone); the lower limits of the lungs extend below the normal level; and there is diminished dislocation of the lower limits on inspiration. The superficial cardiac dullness is diminished or obliterated.

On *auscultation,* the inspiratory murmur is feeble, and is followed by a prolonged, difficult, expiratory sound; rhonchi, sibilant and sonorous, due to the complicating bronchitis, often replace the inspiratory breath sound. During attacks of bronchial catarrh, moist râles may be audible. Though the position of the right margin of the heart may be hard to determine on account of the emphysema unless röntgenoscopy be resorted to, the hypertrophy of the right ventricle is usually indicated by accentuation of the pulmonic second sound. The heart sounds, on the whole, seem distant on auscultation. The most important disturbance in emphysema is undoubtedly the hindrance to the circulation and the strain on the right side of the heart.

The *sputum* varies with the complicating conditions (dry catarrh, moist catarrh, bronchiectasis).

On *x-ray examination,* the abnormal clearness of the pulmonary areas, the low position of the diaphragm and the enlargement of the cardiovascular stripe to the right are striking features.

Diagnosis.—This ought not to be difficult if what has been said above be attended to. In the differential diagnosis, it is necessary to distinguish emphysema (1) from *pneumothorax* (metallic phenomena, process unilateral, röntgenography); and (2) from *bilaterally adherent pleurae with myocardial insufficiency* (higher position of the diaphragm, röntgenography).

Genuine chronic vesicular emphysema will scarcely be confused with acute lung distention if the history of the patient be studied and the course of the disease be observed.

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3. Pneumopathies of Circulatory Origin

Under this heading we include:

(a) Chronic passive congestion of the lungs and stasis bronchitis.
(b) Pulmonary hemorrhage and hemoptysis.
(c) Pulmonary embolism, hemorrhagic infarction of the lung and thrombosis of the pulmonary artery.
(d) Edema of the lungs.

(a) *Chronic Passive Congestion of the Lungs and Stasis Bronchitis*

Definition.—A condition met with in diseases leading to prolonged stasis in the pulmonary veins and resulting in hyperemia and induration of the lungs.

Etiology and Pathogenesis.—Stasis in the pulmonary veins may occur in any condition that causes directly or indirectly a dilatation of the left atrium of the heart. Thus it is common in mitral lesions, and in conditions causing dilatation of the left ventricle, for example, aortic insufficiency and the myocardial insufficiency of myocarditis, adhesive pericarditis, and the chronic cardiopathies of renal and of thyrotoxic origin. The stasis leads to engorgement of the pulmonary capillaries and to a gradual increase in the consistency of the lung substance due to increase of fibrous tissue. The pathological anatomists describe a "red induration" (earlier stages) and a "brown induration" of the lungs (later stages). The alveoli contain a few desquamated alveolar epithelial cells, a few white and red blood corpuscles, and the characteristic hemosiderin-containing "heart-failure cells."

Symptoms.—The patients complain of shortness of breath, especially on exertion, and there is usually cough with mucoid sputum containing desquamated alveolar epithelium filled with a yellow to a blackish-brown-colored ferruginous pigment ("heart-failure cells"). The sputum is occasionally streaked with blood.

On percussion over the lungs, the note may be slightly impaired. On auscultation, the breath sounds are usually impure; they may be feebler than normal or somewhat accentuated, and, owing either to slight edema or to a complicating bronchitis, usually fine and medium-sized moist râles can be heard, especially over the lower lobes, though the findings vary much from day to day.

Röntgenograms show lung areas that are bilaterally and throughout less clear than normal, owing to the general slight condensation of the lung-substance; the hilus shadows are larger and denser than normal.

Chronic passive congestion of the lungs is often complicated by other phenomena common in myocardial insufficiency (*e. g.*, edema of the lungs, atelectasis, hypostatic congestion, hydrothorax, and infarction).

(*b*) *Pulmonary Hemorrhage and Hemoptysis*

Blood in the respiratory tubes may be aspirated from above (nose, pharynx), or result from hemorrhage due to erosion of vessels in the walls of a cavity or of an ulcer (phthisis, lues, paragonimiasis, bronchiectasia, gangrene); from passive hyperemia of the lung (in cardiac stasis, in compression of the pulmonary veins by neoplasms, enlarged glands or aneurisms); from active hyperemia of the lung (in tuberculosis, cancer, echinococcus, or malaria); from rupture of an aneurism or from trauma; from hemorrhagic diathesis (scurvy, hemophilia, purpura, acute leukemia); rarely from vicarious menstruation. In **hemoptysis** or coughing up of blood, these various possible sources as well as hemorrhagic infarction should be considered.

The amount of blood expectorated may vary from a minute quantity, streaking the sputum, to large amounts (100 c.c.; 1 liter; even 3 liters!). The blood is bright red and frothy. There may be fever for 2-3 days after a hemoptysis, due to absorption of blood, or to a complicating inflammation.

In pulmonary tuberculosis a hemoptysis may lead to an extension of the tuberculous process to other parts of the lung, and either a caseous pneumonia or an acute disseminated tuberculosis of the lungs may follow.

In the differential diagnosis of hemoptysis, we must rule out epistaxis, hematemesis, and buccal, pharyngeal and laryngeal hemorrhages.

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(c) *Pulmonary Embolism; Hemorrhagic Infarction of the Lung; Pulmonary Thrombosis*

Embolism of the main stem or of a branch of the pulmonary artery is by no means uncommon; over half of all cases of embolism involve this domain. The most common form of embolus is a **blood clot embolus,** that is, a fragment of a thrombus, detached from its site of formation in the right heart (mitral stenosis, myocardial insufficiency, etc.), or, more often, in one of the body veins (saphenous, femoral, prostatic, uterine, etc.) in acute infections, in the puerperium, and after operations. Other forms of emboli, such as **fat embolus, gas embolus,** and **cell embolus,** are only occasionally met with. The so-called **bland emboli** are sterile; emboli that contain pathogenic bacteria are known as **septic emboli.**

i. Embolism of the Pulmonary Artery or of One of Its Large Branches

Symptoms.—A patient of mine, a young woman, who had suffered for years from mitral stenosis, was talking quietly to her mother while out driving, when suddenly she broke off in the middle of a sentence; the mother, on looking around, saw that her daughter's head had dropped forward and that she was unconscious; in a few moments she was dead. Such a sudden death, due to embolism of the main trunk of the A. pulmonalis, is not uncommon in long-standing cardiac disease, in convalescence from pneumonia, or in the puerperium. The patients may be either very pale when the death is sudden, or cyanotic when they live a little longer. In some instances, the first symptom is extreme dyspnea, accom-

panied by a feeling of anxiety; the patients struggle for breath, and may even cry out; then they become unconscious, the breathing stops and the pulse becomes imperceptible.

When the embolus lodges in the right or, less frequently, the left branch, having passed through the main trunk, death is sometimes just as sudden, but, more often, the patient lives for a few hours; there is marked dyspnea, great anxiety, and, soon, cyanosis; the patient breaks out into a cold sweat, and may remain conscious for a time complaining of headache and vertigo; the pupils dilate, and the eyes protrude; later, patients become comatose and convulsive seizures may precede death. Occasionally, a patient recovers, but often when recovery has begun to seem probable, the symptoms become worse, due to further embolism or to the conversion of a partial obstruction into a complete one from thrombus formation at the site of the embolus.

On examination of the chest, there may be a lagging of the right side of the chest on inspiration, and the breath sounds may be feebler on that side; the area of cardiac dullness usually becomes enlarged to the right.

Diagnosis.—The diagnosis cannot be made with certainty, but it is made very probable if the symptoms above mentioned occur in a patient that is known to have venous thrombosis, or has recently had an operation (laparotomy, prostatectomy), or one in the puerperium, or in the convalescent stage of pneumonia, or under treatment for severe chlorosis. A loud whistling systolic murmur in the second left intercostal space or along the right side of the sternum can occasionally be made out (Litten); it is believed to be a sign of incomplete occlusion of the A. pulmonalis.

ii. Embolism of a Medium-sized Branch of the Pulmonary Artery Causing Infarction of the Lung

The immediate effects of embolism of a medium-sized branch may be slight, or, if the patient suffer from myocardial insufficiency, may be so severe as to resemble those due to embolism of the right or left main branch. In case death does not occur from the embolism there is a danger not incident to embolism of the larger trunks, namely, that of **hemorrhagic infarction.** This occurs only when the pulmonary capillaries are abnormal, either owing to preëxisting passive congestion, or to damage from a septic embolus without previous stasis. The filling of the infarcted area with blood may be due either to collateral flow from neighboring pulmonary capillaries, or to retrograde inflow from the bronchial veins, since, as is well known, the latter empty into the pulmonary veins.

Symptoms.—An embolism not followed by infarct may cause no symptoms during life, as we know from post-mortem examinations of well-studied clinical cases. If infarction occur, the patient complains of a

"stitch in the side," due to the dry pleurisy over the infarct, and of difficulty in breathing. A little later, the sputum becomes streaked with blood or rusty, or there may be an outspoken hemoptysis; on microscopic examination, one sees not only red blood corpuscles, but, also, nearly always, "heart-failure cells." There is usually some fever, and sometimes a chill, and these symptoms may lead to the false diagnosis of croupous pneumonia. The fever may occur even when the infarction is due to a bland embolus; it may then be the result either of absorption of blood or of a secondary infection.

On percussion and auscultation, there is dullness over the infarcted area; the breath sounds, at first indefinite, soon become bronchial in type; crepitant râles are audible; and, frequently, a pleuritic friction sound can be heard. In the röntgenogram, a shadow, usually sharply circumscribed, can be made out, though if the passive congestion be extreme, or if there be associated edema of the lung, the outlines of the shadow may not be sharp.

Hemorrhagic infarction occurs more often in the lower lobe of the right lung than in any other part.

In favorable cases, the temperature may soon become normal, the sputum ceases to be bloody, and the physical signs gradually disappear. In the unfavorable cases, death may occur from cardiac failure, from abscess formation or from gangrene. Occasionally, an empyema develops, or a pneumothorax occurs. A patient doing well, after an embolism, may succumb later from repeated embolic attacks.

Differential Diagnosis.—We must try to distinguish infarction (1) from *simple dry pleurisy;* (2) from *lobar pneumonia;* (3) from *pulmonary tuberculosis* (anamnesis, sputum, Calmette, x-ray); (4) from *tumor of the lung* (röntgenogram); (5) from *echinococcus cyst* (x-ray, situation in upper lobe or in left lung, complement-fixation test).

iii. Embolism of the Smaller Branches of the Pulmonary Artery

A single embolus in a small branch does no harm and causes no symptoms, except, of course, when it carries pathogenic bacteria or tumor cells, in which event a metastatic abscess or a local neoplasm may develop.

Multiple embolisms of small branches of the A. pulmonalis are most often due either to air bubbles (opening of a large vein at surgical operation), or to fat droplets (after bone injury); they may be very serious indeed, often causing death either suddenly or after a few hours.

Symptoms.—In *air embolism*, there may be a sudden attack of dyspnea with cyanosis after opening a large vein; the surgeon may hear the gas enter the vein. The patient quickly becomes unconscious and may have convulsions. Death may occur at once, or after a few hours. Recovery is rare. A bubbling murmur may be audible over the right heart, since

the right ventricle may be full of air or bloody froth; in the area of cardiac dullness the percussion note may become tympanitic.

In *fat embolism*, though the emboli lodge in the smaller branches of the pulmonary arteries, the symptoms resemble those of gradual occlusion of the main trunk of the A. pulmonalis. (See above.) The patient, a few hours after a bone injury, or after a severe burn, begins to have dyspnea, which gradually increases in severity. There is a general cyanosis. The patient has an anxious look. On physical examination of the lungs, there may be nothing to make out, except slight signs of pulmonary edema (*q. v.*). Recovery is not uncommon if the emboli be not too numerous. In the severer cases, death occurs in a few hours or days. Now and then, fat droplets pass through the lungs, enter the general circulation, and may give rise to embolism of the cerebral, retinal, or renal arterioles. In cases that recover, the emboli disappear, partly through saponification of the fat by the blood, partly through ingestion by phagocytes.

iv. Thrombosis of the Pulmonary Artery or of Its Branches

Autochthonous thrombosis of the main trunk or of the right or left branch is rare, but does occur occasionally, especially in children after severe intestinal catarrh (Beneke) or after measles (Staehelin); the lesion also may occur as an agonal phenomenon. During life, the signs are usually believed to be due to a bronchopneumonia and only at autopsy is the true nature of the lesion revealed.

Most of the described thromboses of the artery were not primary, but were either thrombotic extensions of emboli, or were only the emboli themselves derived from distant thrombi in veins (Lubarsch). Multiple thrombi are sometimes found in the smaller branches of the pulmonary artery after inhalation of poisonous gases (*e. g.*, phosgen); the diagnosis cannot be made with certainty during life.

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(*d*) *Edema of the Lungs*

In edema of the lungs, serum escapes from the capillaries and not only saturates the interstitial tissue but also enters the pulmonary alveoli. It may be (1) inflammatory, as in pneumonia; or (2) non-inflammatory or mechanical, due to cardiac failure, especially when the left ventricle fails before the right (W. H. Welch); the latter is often agonal, and is especially common in mitral stenosis, in acute intoxications and infections, and in diseases associated with hydremia (chronic nephropathies, pernicious anemia, etc.). According to Sahli, an increased permeability of the vessel walls is even more important than the failure of the left heart; in some cases, neural influences appear to play a part. Clinically, we may be unable to distinguish the *mechanical,* the *inflammatory,* and the *neural edemas* from one another. Acute edema of the lungs occasionally follows thoracentesis.

Symptoms and Signs.—The onset is usually heralded by dyspnea and cyanosis; the extremities are cold and the patient breaks out into a cold sweat, the face assuming an anxious appearance. In outspoken cases of acute and peracute edema, the sputum is very characteristic, being copious, thin, frothy and tinged pink owing to the admixture of blood. Loud tracheal râles (the "death-rattle") may be audible. The frothy, blood-stained fluid may well up into the mouth and out through the lips in large quantities; this fluid is rich in protein and may coagulate spontaneously in the sputum cup.

The percussion note varies according to the degree of edema. When this is slight there may be no change, or only slight tympany. If it be marked, and especially if the edema be chronic, the note may be dull. Crepitant or loud moist râles are nearly always audible on auscultation; sometimes there is only loud roughened breathing without râles. In the röntgenogram, the lung area is not as clear as normal, being diffusely clouded or indistinctly mottled.

In *inflammatory edema,* there is fever, a strong pulse, and usually a polymorphonuclear leukocytosis.

In *non-inflammatory edema,* fever is absent, the pulmonary second sound is exaggerated, and the pulse is usually small and frequent. The history of the case (cardiac disease, renal disease, arterial hypertension) helps in the diagnosis. A recurring form of acute pulmonary edema is not uncommon in mitral stenosis and in arteriolar nephropathy.

Diagnosis.—This is easy when dyspnea is associated with frothy, blood-tinged sputum, rich in protein. When the typical sputum is absent, the diagnosis may be difficult and the condition may be confused with hypostatic congestion or with atelectasis. When the condition of a patient favors the development of a pulmonary edema, a close watch should be kept on the lungs; should crepitation appear and begin to spread rapidly, prompt and energetic therapy may prevent an attack.

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4. Pneumopathies Due to Foreign Bodies and Parasites

Under this caption may be included (a) the pneumonoconioses and (b) parasitic invasions of the lungs.

(*a*) *The Pneumonoconioses*

Definition.—The diseases of the lungs due to inhalation of dust of various sorts are called the pneumonoconioses. The dust gives rise to chronic bronchitis and to interstitial inflammations of the lung that lead

to fibrosis (*cirrhosis pulmonum*). Bronchiectasis and emphysema often develop. The diseases are often complicated by tuberculous infection.

Varieties of Pneumonoconiosis.—Three main varieties are distinguishable, namely:

(1) *Anthracosis pulmonum*, due to carbon or coal-dust, met with in coal-miners, chimney-sweeps, stokers, and workers in graphite.

(2) *Chalicosis pulmonum*, due to stone-dust, and met with in stone-cutters, slate-workers, polishers, etc. The gold-miner's phthisis of South Africa seems to belong here.

(3) *Siderosis pulmonum*, due to iron-oxid-dust, met with in file workers, iron-workers, scissors-grinders, mirror-makers, workers in wall-paper factories, etc.

Similar lung diseases occur in persons following other occupations (millers, bakers, carpenters, weavers, cigar-makers, potters, fertilizer-makers, etc.).

Disposition.—It is a remarkable fact that certain only of the workers become affected. There would seem, therefore, to be a special disposition to attack. This disposition is increased by any previous affection of the bronchi or of the lungs. The disease has been experimentally studied by Arnold (1885) and by Tendeloo (1902). One of the best accounts in English will be found in Oliver's "Diseases of Occupation" (1908).

Symptoms.—While the dust is being inhaled, the symptoms of bronchitis develop and the sputum contains the dust particles. As a rule the bronchitis ceases soon after removal of the patient from the harmful occupation, but it may continue even after removal, especially if bronchiectasis and emphysema have already developed. Occasionally, a putrid bronchitis complicates the picture. When the disease has led to chronic interstitial inflammation of the lungs, there is dullness on percussion, and moist râles are audible on auscultation, the upper lobes being symmetrically involved on the two sides (the reverse of what occurs in fibroid tuberculosis, in which one side is more involved than the other). The patients are usually pale, suffer from cough, and may have "asthmatic" attacks. Many of them are erroneously believed to be tuberculous, especially if there be cavity formation with nummular sputum. It must not be forgotten, however, that pneumonoconiosis and tuberculosis not infrequently coexist.

Röntgenograms show a coarsely granular, evenly distributed, mottling of the upper parts of the lung areas, the two lungs being equally affected. The appearance is not unlike that of miliary tuberculosis, but the markings are coarser.

In the later stages, the signs of **cirrhosis of the lung** can be made out, namely, retraction of the chest on the affected side, increased vocal fremitus, dullness on percussion, and bronchial breathing with moist [illegible]. The right heart is hypertrophied and the pulmonic second sound [illegible]

ated. In the severer forms, the right ventricle dilates and relative tricuspid insufficiency develops. The bronchial lymph glands become filled with dust transported through the lymph channels; sometimes these glands soften and break down, rupturing into the bronchi, the blood vessels, the pericardium or the esophagus. Cicatrix formation may lead to traction-diverticulum of the esophagus, or to tracheal or bronchial stenosis. Occasionally a fibrous mediastinopericarditis develops as a result of pneumonoconiosis.

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(*b*) *Parasites of the Lung*

Aside from bacterial invasions of the lungs, invasions by actinomyces, streptothrix, aspergillus, mucor, thrush fungi, etc., may occur. Pigeon-feeders are especially prone to pseudotuberculosis aspergillina, described by French authors as *maladie des ganeurs des pigeons.*

Of the animal parasites that invade the lung, echinococcus and paragonimus are the more important.

Echinococcus cyst is most often met with in the right lower lobe. The parasite usually reaches the lung as an embolus, having reached the right heart either through the vena cava superior or through the vena hypogastrica. Sometimes a cyst of the liver breaks into the right pleural cavity and then involves the lung. The diagnosis depends on (1) the röntgenogram, (2) the complement-fixation test, or (3) upon finding membrane or hooklets in the sputum.

The *Paragonimus westermanni* is the cause of the *endemic hemoptysis* of Japan and other Oriental countries. (For a description, see section on Sputum.)

An amebic abscess of the liver is sometimes emptied through the lung and the *Entameba histolytica* is discoverable in the sputum.

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5. The Neoplastic Pneumopathies

(*Tumors of the Lung*)

Tumors of the lung may be primary in the lung substance or bronchi (carcinoma); more often they are metastatic through the blood (sarcoma), or reach the lung by extension directly, or through th channels (sarcoma of the thymus, lymphosarcoma, carcinoma e Benign tumors (teratoma, dermoid cyst, fibroma, adenoma, li teoma, chondroma) are clinical and pathological rarities.

Cancer of the lung, when primary, arises most often from t glands of a bronchus, occasionally from the surface epithe

bronchus or of a pulmonary alveolus. When a cancer *begins at the hilus of a lung* it may extend as a compact mass into the adjacent lung tissue, or it may grow out into the lymphatics (either those ensheathing the bronchi, or those in the interstitial tissue of the lung). But cancer may begin in the *middle of a lobe* and form a sharply circumscribed mass there, or it may *diffusely infiltrate a lobe,* roughly resembling the involvement in a caseous pneumonia. Metastases may involve the pleura, the bronchial glands, or, sometimes, the mediastinal and the supraclavicular glands.

Primary LYMPHOSARCOMA of the lung is not uncommon among miners. Secondary (metastatic) tumors of the lung are much more common than primary tumors. They are usually multiple and often involve both lungs.

Symptoms.—At onset the symptoms may not be at all characteristic. The patient may complain of pain or discomfort in the thorax, of cough and sputum, or of an inexplicable dyspnea. Occasionally, the signs of pleurisy, of dysphagia, or of hoarseness and paralysis of a recurrent laryngeal nerve first excite attention. There may or may not be fever of low grade.

On *physical examination,* there may be lagging of one side of the chest on inspiration, or signs either of a pleural effusion or of retraction on one side. Pressure signs may be visible on inspection (collateral circulation).

On palpation, percussion and auscultation, we may find dullness, with enfeebled breath sounds, and lessened vocal fremitus, without râles. Not infrequently, the signs of a pleural effusion, of a mediastinal mass, or of a bronchiostenosis will be demonstrable.

The *sputum* may or may not be characteristic. Raspberry-jellylike sputum is very suspicious. Hemoptysis occasionally occurs. Large fat droplets in the sputum are suggestive (degeneration of tumor cells). Sometimes actual tumor-particles can be found in the sputum. If tumor be suspected, some of the sputum should be hardened, sectioned and stained, and areas of carcinoma- or sarcoma-tissue looked for.

When *pleural effusion* is present, the fluid obtained by exploratory puncture should be carefully examined. A hemorrhagic effusion usually indicates either tuberculosis or carcinoma. (See Tumors of the Pleura.) Cytological study of the sediment may reveal the presence of tumor cells (sheets of cells, "seal-ring" cells).

In *röntgenograms* the findings may be characteristic and decisive, especially in tumors beginning at the hilus. One sees a spherical or irregularly-shaped mass from which jagged processes radiate out into the surrounding lung area. In metastatic carcinoma, multiple shadows may be scattered through both lungs, usually most numerous in the right lower lobe.

Diagnosis and Differential Diagnosis.—Many mistakes are made. The

Fig. 175.—Tumor of Lung. (X-ray Dept., J. H. H.)

condition is often overlooked when present; a positive diagnosis of neoplasm is sometimes made when no tumor exists.

Errors of omission are less likely if the clinician will think of the possibility of tumor of the lung in obscure intrathoracic disease. A persistent pleurisy, especially if the effusion be hemorrhagic, a gradually developing bronchiostenosis, a raspberry-jelly sputum in an old person, a mediastinal growth, or a progressive cachexia associated with cough and dyspnea, should certainly excite suspicion. This suspicion will be strengthened if the physical signs above described (circumscribed dullness, suppression of breath sounds, diminished fremitus, absence of râles) be found, or if the röntgenogram be characteristic. The occurrence of enlarged supraclavicular glands may be helpful in the diagnosis. I was once called to Texas, to try to give relief to an elderly miner, who was supposedly suffering from pulmonary tuberculosis, and who had begun to have severe neuralgic pains in the neck. On examination, I found a hemorrhagic pleural effusion on one side, suggestive lung signs, and enlarged supraclavicular glands that rapidly grew in size. On excision of one of the glands for diagnosis, the histological study revealed a lymphosarcoma. On another occasion, I saw in Virginia an elderly miner, supposedly suffering from uremic asthma. His blood pressure was only

slightly elevated, there was a trace of albumin and a few casts in the urine, and his heart was negative; a routine physical examination brought to light a chain of enlarged lymph glands in the right neck, and suspicious lung signs. The glands rapidly enlarged and the patient died a few weeks later.

In some cases, a positive diagnosis becomes possible through finding particles of tumor in a pleural effusion or in the sputum, through histological examinations of a supraclavicular gland, or through actual bronchoscopic inspection.

If neoplasm be thought to be present, we should try to determine its site and its origin, whether it be single or multiple, whether primary or secondary, and, when possible, its exact nature.

In the differential diagnosis we must rule out: (1) *aneurism of the*

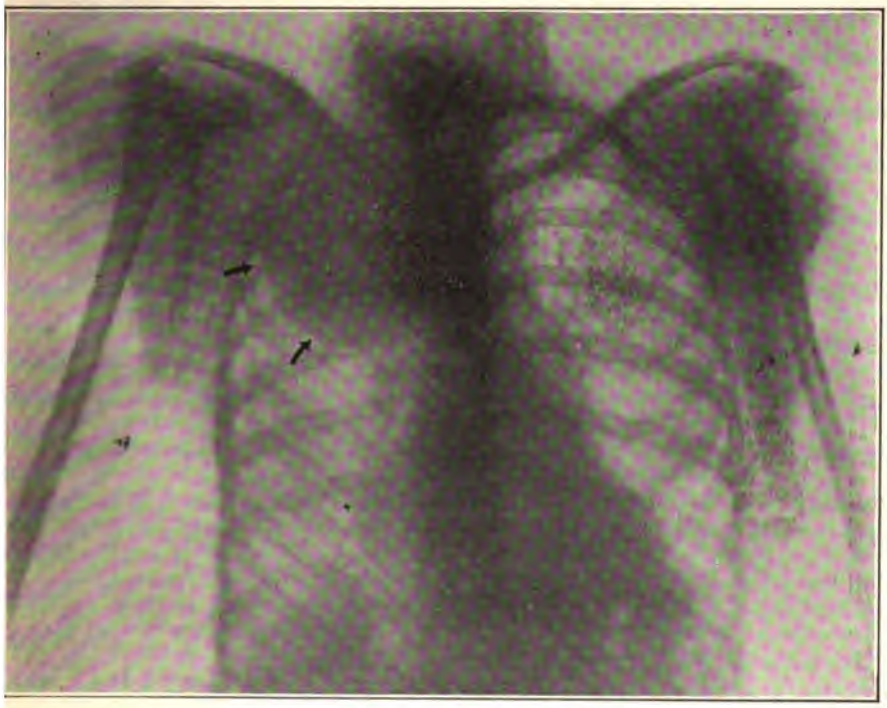

Fig. 176.—Intrathoracic Tumor; Probably a Teratoma. Note the Smooth Contour. (X-ray Dept., J. H. H.)

aorta (röntgenoscopy, positive Wassermann); (2) *mediastinal tumors* (*q. v.*); (3) *pulmonary tuberculosis* (search for bacilli, absence of tumor cells and fat droplets from sputum, röntgenography; histology of excised gland); (4) *echinococcus cyst* (röntgenography, complement-fixation test). The possibility of confusion with (5) *infarct of the lung*, (6) *syphilis of*

the lung, (7) *actinomycosis*, and (8) *chronic abscess* and *gangrene* should also be borne in mind.

In the United States, Dr. I. Adler of New York has had a large experience with tumors of the lung, the results of which, together with a review of the literature, are recorded in his excellent monograph.

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F. Diagnosis of the Principal Diseases of the Pleura

The principal diseases of the pleura include:

1. Inflammations of the pleura (pleuritis);
2. Circulatory disturbances involving the pleura (hydrothorax and hemothorax);
3. Air or gas in the pleural cavity (pneumothorax); and
4. Tumors of the pleura.

1. Inflammations of the Pleura (Pleuritis, Pleurisy)

Pathology.—Inflammations of the pleura may be (a) *simple* (due chiefly to pyogenic microörganisms—streptococci, pneumococci, influenza bacilli, etc.), in which case they may be acute or chronic; or (b) *specific* (tuberculosis, luetic, etc.).

The exudate in acute pleuritis may consist chiefly of *fibrin* (dry pleurisy or pleuritis sicca), or of *fluid* (pleurisy with effusion or pleuritis exudativa). In the latter case, the exudate may be *serous, serofibrinous, hemorrhagic* or *purulent.* A purulent effusion is sometimes spoken of as an empyema or pyothorax.

Such pleuritides may have their origin in:

(1) Inflammations or infarcts of the lung, with extension to the pleura;

(2) Inflammations of neighboring organs extending through (pericardium, bronchial lymph glands, peritoneum), or perforations from abscess of the liver or spleen, from ulcer of the stomach, or from carcinoma of the stomach or of the esophagus;

(3) A general infection (septicemia, pyemia, articular rheumatism, scurvy, smallpox; or

(4) A metastatic infection from some local focus (tonsillitis, sinusitis, etc.).

An acute pleurisy may end in complete *absorption* of the exudate, in the formation of *adhesions* (organization of the exudate), or, in *chronic pleurisy with thickening.* Sometimes we meet with encapsulation of an exudate. Calcification or ossification of the pleura occasionally occurs.

Of the specific pleurisies, tuberculosis is by far the most common. Tuberculous pleuritis usually arises by extension from the lungs or from the bronchial glands. Syphilis and actinomycosis of the pleura are rare.

The clinical recognition of the existence of pleurisy depends chiefly upon the results of physical examination, less upon the subjective symptoms present. The diagnostic procedure is divisible into two parts; (1) the detection of the signs of anatomical lesion; and (2) the etiological or bacteriological diagnosis.

For clinical purposes, three main types of anatomical lesion are distinguishable:

(a) Dry or plastic pleurisy (*pleuritis sicca*);
(b) Pleurisy with effusion (*pleuritis exudativa*);
(c) Chronic pleurisy with adhesions or with pleural thickening (*pleuritis chronica productiva*).

(*a*) *Dry or Plastic Pleurisy*

(*Pleuritis sicca*)

Definition.—An inflammation of the pleura in which the exudate consists chiefly of fibrin.

Fig. 177.—Areas in Which Pain and Hyperalgesia Were Present in a Case of Diaphragmatic Pleurisy. Shaded Area on Left Shoulder is in the Cutaneous Distribution of the Fourth Cervical Nerve, and is an Evidence of the Conduction of a Stimulus from the Diaphragm by the Phrenic Nerve, Which Leaves the Spinal Cord with the Fourth Cervical Nerve. Phrenic Nerve Contains Afferent Fibers as Well as Efferent (Motor), and it is in all Probability by the Former that the Stimulus is Conveyed to Center of Fourth Cervical Nerve in Cord. Shaded Area in Abdomen is in Region of Distribution of Eighth and Ninth Thoracic Nerves. (After J. Mackenzie, "Symptoms and their Interpretation," published by Shaw & Son, London.)

Etiology.—By far the most common cause of dry pleurisy is a tuberculous infection. But it may follow trauma, or may occur temporarily at the onset of a lobar or a lobular pneumonia, in carcinoma, or as a forerunner of a subphrenic abscess.

Symptoms and Signs.—The patient usually complains of *pain* in the chest on the side affected, most often in the lower axilla, and tries to lessen it by diminishing the respiratory movements on that side. There may be a little *cough*, with slight *fever*. *Friction fremitus* may be palpable. On auscultation, a *friction rub* (*q. v.*) of variable intensity is audible, and is the main criterion in diagnosis. Such pleural friction is usually loudest in regions in which the excursion made by the visceral pleura over the parietal pleura during respiration is greatest, that is, at the lower margins of the lung and in the axillary line. The sound is a more or less interrupted one and is usually audible during both expiration and inspiration. It is increased by pressure on the stethoscope.

Occasionally, a dry pleurisy may be demonstrable at one apex (though a rub here i owing to the minimal movement), or i diaphragmatic pleura (friction rub occ ally, though rarely, audible near diaphrag attachment; hiccough common; pain lower margin of the thorax, especially o ing or on retching, sometimes referre

abdomen; sudden contraction of upper part of M. rectus abdominis on diseased side on deep inspiration, or so-called "respiratory abdominal reflex" of R. Schmidt; pain on pressure at certain points, namely, (1) between the sternal and the clavicular attachment of the M. sternocleidomastoideus, (2) the sternal margin of the first intercostal space, (3) the junction of the parasternal line with a line corresponding to the course of the 10th rib, (4) line of the diaphragmatic attachment, and (5) the spines of the 4th and 5th cervical vertebrae).

Care should be taken not to confuse a friction rub with (a) skin sounds, from slipping of the stethoscope, (b) muscle sounds, or (c) atelectatic crackles.

A dry pleurisy may disappear in a few days, or it may last for weeks or even for months. It is always important to search for what "lies behind it."

(*b*) *Pleurisy with Effusion*

(*Pleuritis exudativa*)

Definition.—An inflammation of the pleura associated with a fluid exudate; the fluid may be serous, serofibrinous, serohemorrhagic, purulent, or putrid.

i. Pleurisy with Serous or Serofibrinous Effusion

(*Pleuritis serosa and Pleuritis serofibrinosa*)

Etiology.—The majority of cases are due to tuberculous infection. Bacteriological examinations of the centrifugate by means of stained smears or by cultural methods in the tuberculous cases may be negative, but inoculation of a guinea-pig with the sediment is usually positive. Even when bacteria other than tubercle bacilli are demonstrable in the centrifugate, the possibility of a mixed infection should not be lost sight of.

Certainly 80 per cent or more of all serofibrinous pleurisies have a tuberculous basis. In the 20 per cent (or less) that are non-tuberculous, any one of several varieties of bacteria may be responsible. Most often, perhaps, the pneumococcus is found. Streptococcus and staphylococcus pleuritides are also not uncommon. More rarely, the B. typhosus, the B. diphtheriae, the meningococcus, Friedländer's bacillus, or other bacteria may be met with.

When the pleuritis is the only local manifestation of the infection it is said to be "primary" or "idiopathic"; when, however, it is discoverably due to propagation from an inflammation in the neighborhood of the pleura, or to metastatic deposition in the pleura of bacteria brought by the blood current from some distant focus of infection, it is said to be "secondary." In the last analysis, we must believe that all pleuritides are secondary; we call them "primary" only when we cannot discover the mode of infection of the pleura.

Symptoms and Signs.—In some instances, the onset is acute, with stitch in the side, chill, fever, tachycardia and dyspnea; in other instances,

are overfull, and the apex beat of the heart, if visible, can be seen to be displaced toward the side opposite the effusion.

On *palpation,* the vocal fremitus will be found to be absent, or greatly diminished, over an effusion; just above the level of the fluid, it may be exaggerated owing to the proximity of compressed lung; still higher, it may be normal. In testing the vocal fremitus in a woman, we ask her to pitch her voice low when counting "one, two, three" or saying "ninety-nine," since the fremitus is most marked when the pitch of the voice corresponds to the *Eigenton* of the lung (F. v. Müller). It should be remembered that in emphysema, and in old people with rigid thorax, the vocal fremitus is often indistinct even when the pleurae are normal. Should the pleura become thickened, the vocal fremitus may remain absent or feeble even after the absorption of the effusion.

Dislocation of the heart to the right or to the left by an effusion in a pleural cavity can often be suspected through determination of the position of the apex beat by palpation.

On *percussion,* if the effusion reach any considerable size (say 400-600 c.c.), dullness or flatness, with total absence of tympany, can be made out over it. The upper limit of flatness (light percussion) and increased resistance on percussion assumes a typical curved form (except when the effusion is so large as to cause dullness over the whole side from base almost to apex). Thus, in medium-sized effusions, the upper limit of dullness extends from the spine upward and lateralward to reach its highest level in the posterior axillary line, whence it curves downward and forward toward the middle line in front (Ellis' line, Damoiseau's curve). Sometimes the line takes the form of a letter S turned on its side.

In the lower back, close to the spine on the healthy side, there is a triangular area of relative dullness with base below and apex in the spine above the level of the effusion. This is known as the *paravertebral triangle of dullness* (*Grocco's triangle, v. Koranyi's triangle*). Authors vary in their explanations of the origin of this dullness, but the evidence seems to favor the view that it is due to dislocation of the posterior inferior mediastinum and compression of the healthy lung. The sign is of some value in the differential diagnosis of pleural effusion from pneumonia of the lower lobe.

In the lower back, close to the spine on the diseased side, there can be demonstrated a triangular area of relative resonance after the patient has coughed and breathed deeply; the apex of the triangle is below and the base above (*Garland's triangle*). The note is not perfectly clear owing to the fact that the lung is compressed and, besides, there may be a very thin layer of fluid over it (Sahli), but it is relatively clear in contrast with the flat note lateral from it (below Ellis' line). Garland's triangle is not present when the exudate is large. In lobar pneumonia such a triangle of relative resonance near the spine is never met with.

Fig. 178.—Grocco's Sign—Aortic Aneurism; Hydrothorax on Right Side.
(Med. Service, J. H. H.)

Dullness or flatness on light percussion in the upper part of Traube's semilunar space is an important diagnostic sign of beginning accumulation of fluid in the left pleural cavity. On the right side, dullness due to effusion may fill up the cardiohepatic angle and, on superficial examination, mislead the physician into thinking it is due either to an effusion into the pericardial cavity, or to a dilatation of the right side of the heart.

The upper limit of dullness due to pleural effusion changes a little on deep inspiration, and on change of posture, unless it be encapsulated; the change is rarely great, however.

One striking feature on more forcible percussion over an effusion deserves especial mention, namely, the increasing intensity of the dullness (flatness) and of the feeling of resistance on percussing from above downward; on immediate percussion with the finger tips, the increased feeling of resistance may be most easily experienced.

On percussing over the lung just above the upper level of the effusion, a zone of loud tympanitic resonance is met with (Skodaic resonance). If an effusion is large, Skoda's resonance may be elicitable in the infraclavicular region, owing to the relaxation of the lung. Sometimes the pitch changes with the phases of respiration (Williams' "tracheal tone"), or on strong percussion a "cracked-pot sound" may come out.

When the effusion is on the right side, the lower edge of the liver may be found, on percussion, to lie lower than the costal margin.

Changes in the size of an exudate during absorption are best followed by *mensuration* with a tape, rather than by percussion (Staehelin). Four measurements should be carefully made, namely, that of each half of the thorax above the nipple and also at the level of the xiphoid. As an effusion diminishes in size, both halves of the thorax grow smaller, but the reduction is much more marked on the side of the effusion. In the late stages of a pleuritis, the dimensions of the diseased side may be less than those of the healthy side, owing to retraction of the thorax.

On *auscultation*, a friction-rub may be audible at the very beginning; even after an effusion has developed, a rub may be audible near its upper limit; as the fluid becomes reabsorbed a rub may become audible at the former site of an effusion as soon as the visceral and parietal layers of the pleura again come into contact.

Over an effusion the breath sounds may be diminished or entirely absent according to the thickness of the layer of fluid. Occasionally, distant bronchial breathing, bronchophony, and râles are audible through an effusion, especially in children. On the healthy side, the breath sounds may be exaggerated owing to "vicarious emphysema." The voice sounds are usually distant behind an effusion; as an effusion is developing, a strange, high-pitched, bleating or nasal quality may characterize the voice sounds auscultated at the upper margin of the effusion (egophony). It has been asserted that the whispered voice grows ever less distinct as an exudate grows richer in cells (Baccelli's sign of empyema); but the sign is notoriously unreliable, and it is better to study the cell count of fluid obtained by exploratory puncture.

It is nearly always, if not always, advisable to make an exploratory puncture when pleuritis with effusion is either known, or suspected, to exist. The chemical, bacteriological, serological, and cytological methods of studying the fluid obtained are described in the section on Exploratory Punctures (*q. v.*).

On *röntgenoscopy*, it is sometimes possible to discover small pleural effusions not demonstrable by percussion. If the effusion be confined to the pleural sinus, it is necessary carefully to adjust the tube and the direction of the transillumination if the shadow is to be discovered. It is best to have the patient assume a sitting or a standing posture, if he be not too ill. In larger effusions, the shadow is seen to be highest in the lateral part of the thorax and lowest and most intense near the spine behind and near the sternum in front. The upper limit of an effusion appears in the röntgenogram as an indistinct concave border to the shadow, very different from the margin of a pneumonic infiltration or of a tumor.

The dislocations of the organs (heart, mediastinum) are easily visible fluoroscopically. The lung area on the healthy side may be less clear than

normal if an effusion be large, owing partly to compression, partly to hyperemia. When the effusion is small, the lung on the affected side may be unusually clear owing to "vicarious emphysema."

Several ATYPICAL FORMS of serofibrinous pleurisy must be mentioned, including (1) the diaphragmatic form, (2) the interlobar form, (3) the mediastinal form, and (4) the pleurisy that is a part of a polyserositis.

In *diaphragmatic pleurisy with serofibrinous effusion,* the fluid accumulates between the lower surface of the lung and the diaphragm. The symptoms at onset resemble those of dry pleurisy in this situation. (See Pleuritis sicca.) On x-ray examination, the shadow due to the effusion may be visible.

In *interlobar pleurisy with serofibrinous effusion,* the fluid may be poured out in the cleft between two lobes, and, owing to adhesions, be prevented from reaching the general pleural cavity. A zone of dullness varying in width with the volume of the effusion can be made out on the surface of the chest in regions corresponding to the junctions of the lobes. There may be Skodaic resonance above and below the narrow zone of dullness, owing to relaxation (or compression) of the adjacent lung tissue. The breath sounds are feeble over the zone of dullness, whereas above and below it the breathing may be almost bronchial in type. Moist râles may be audible in the adjacent lung. The condition may be mistaken for tumor of the lung, pneumonic infiltration, lung abscess, or interlobar empyema. The röntgenogram is of great aid in distinguishing an interlobar effusion from tumor or pneumonia, as is also exploratory puncture with a long needle in the axillary line over the zone of dullness; the latter will also differentiate between a serofibrinous and a purulent exudate. (See Interlobar Empyema.) Occasionally, an interlobar exudate breaks through into the general pleural cavity at one end of an interlobar cleft, but remains circumscribed there, owing to adhesions in the neighborhood; in this way arises the so-called "shirt-stud-shaped effusion" of Sabourin.

In *mediastinal pleurisy with serofibrinous effusion,* the fluid collects between the mediastinal and the pulmonary pleura and recognition may be very difficult. It may be located in the anterior or in the posterior region of the chest, on either the right or the left side. Good accounts of this form of pleuritis will be found in the articles of Frick and of Savy.

In *serofibrinous pleurisy as a part of a polyserositis,* there may be fluid also in the pericardial cavity, in the peritoneal cavity, or in [illegible] Such a polyserositis is most often tuberculous, but a non-tuberculous does occur. (See also Pick's Syndrome.)

Diagnosis.—The local signs of pleurisy with effusion are very c istic. (See above.) A serofibrinous exudate can be distinguis (1) the purulent exudate of an *empyema,* and (2) from the tran a *hydrothorax,* by study of the fluid obtained by exploratory pun

etiological diagnosis can also often be made from the study of this fluid, and from the study of the body as a whole.

In the differential diagnosis, we must also rule out (3) *pneumonia* (vocal fremitus usually increased, topography of dullness and its slightly tympanitic character, crepitant râles, no marked dislocation of adjacent organs, "dry tap," röntgenogram; sometimes a pneumonia and a pleurisy with effusion coexist); and (4) *pleural thickening.* (See below.)

ii. Pleurisy with Serohemorrhagic Effusion

The local signs are like those of pleurisy with serofibrinous effusion. On exploratory puncture, the serohemorrhagic character is discovered. Such an exudate points nearly always to either a tuberculous or a neoplastic etiology, just as do chylous and pseudochylous pleural exudates. In rare instances, we may meet with a serohemorrhagic exudate in pneumococcus pleuritis or in a pleurisy from any cause occurring in association with a hemorrhagic diathesis.

iii. Pleurisy with Purulent Exudate

(*Pleuritis purulenta, Pleuritis suppurativa, Empyema pleurae*)

Etiology.—Pleuritis with purulent exudate is usually secondary to lobar pneumonia (pneumococcus infection) or to pulmonary phthisis (tuberculous infection); sometimes, especially in children, it is secondary to a bronchopneumonia due to streptococcus infection. In the careful studies by Dr. F. T. Lord of Boston of the pus from empyema cases, the pneumococcus was found to be the cause in 39.4 per cent, the streptococcus in 20.4 per cent, the staphylococcus in 3.6 per cent, and mixed infections in 16 per cent; in 18.2 per cent the pus was sterile. When no bacteria grow on media suitable for the pneumococcus and for ordinary pyogenic organisms, the etiological agent may have been the B. tuberculosis (guinea-pig inoculation), or an anaërobic organism (see Putrid Empyema); or a pneumococcus may have been present and been killed off before the culture was made.

Symptoms and Signs.—Empyema pleurae is always the result of a severe infection; either the microörganism causing the pleuritis is especially virulent or the patient's resistance is low, or both conditions simultaneously obtain. The severity of the general symptoms is further dependent upon the absorption of the disintegrating leukocytes of the pus shut up in the pleural cavity. It is very important to distinguish clinically between a purulent and a nonpurulent effusion in cases of pleuritis, for, in empyema, the pus cavity should be promptly evacuated, and provision made for thorough drainage.

The GENERAL SYMPTOMS may be so severe as to excite suspicion of a purulent exudate. Intermittent fever, tachycardia, sweats, and chilly

sensations are common, and there are often repeated severe chills. The patients grow rapidly pale and begin to emaciate. There is usually an outspoken hyperleukocytosis with marked relative increase in the polymorphonuclear neutrophils in the blood. It should be remembered, however, that in children, in the aged, and in decrepit patients of any age, the onset of empyema may be insidious and without symptoms directing the physician's attention to the respiratory apparatus; in such cases, the thorough routine examination alone saves the clinician from overlooking the important local physical signs.

On PHYSICAL EXAMINATION, the findings, except on exploratory puncture, may be indistinguishable from those described above for pleurisy

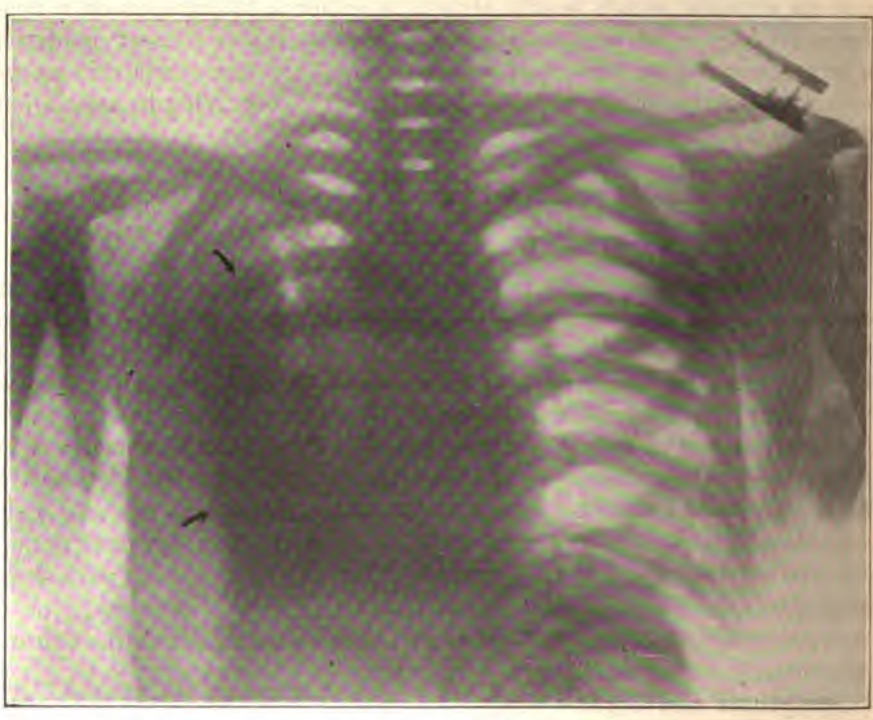

Fig. 179.—Pleurisy and Empyema. (X-ray Dept., J. H. H.)

with serofibrinous effusion (*q. v.*). Occasionally, there is edema of the wall of the chest opposite the exudate, or a pulsating bulging (*empyema pulsans*) may be visible, the latter when it occurs being almost always on the left side. An *encapsulated empyema*, or an *interlobar empyema*, may be small and yield but few physical signs; here, a röntgenogram is of the greatest help in the recognition of the exact position and size of the exudate, and gives us the clew to the proper site for exploratory puncture. The same is true of *diaphragmatic* and of *mediastinal empyema*. In the

röntgenogram the "hanging shadow" extending from the region of one shoulder toward the heart is characteristic of interlobar exudate.

Bilateral empyema is rare, but does occasionally occur.

Empyema in connection with pneumonia (see Gerhardt's studies) may either accompany the pneumonic process (*parapneumonic empyema*), or it may be a sequel to it (*metapneumonic empyema*).

A *tuberculous empyema* is usually secondary to pulmonary tuberculosis, but it may be met with as a complication of caries of a rib or of the spine. It is very often accompanied by pneumothorax (*pyopneumothorax*).

Empyema should be suspected whenever in the course of pneumonia there is a change in the patient's condition with appearance of a paroxysmal, non-productive cough, chills, sweats and a more remittent type of fever. The physical signs may readily permit one to localize the purulent accumulation; but in interlobar or other encapsulated forms the diagnosis is often difficult. Exploratory puncture should be resorted to early. Röntgenograms may yield valuable information. Frequently, however, the condition is first thought of when, at the end of the usual duration of the pneumonia, the fever and leukocytosis persist. Delayed resolution explains a number of such cases, but this diagnosis should never be made until every effort has been put forth conclusively to rule out the possibility of an empyema or of a tuberculous pneumonia.

It is a great pity that an empyema should ever be overlooked, for it is rare that the pus undergoes spontaneous absorption, except in the parapneumonic form, and occasionally in the empyemas of children. It is not uncommon to receive in hospitals patients that have had an undetected empyema for weeks, and who, through the long-continued infection and high fever, have become extremely prostrated and emaciated. Such patients may have already suffered general amyloid change (spleen, kidneys, intestines); some of them have metastatic infections (arthritis, endocarditis, meningitis, brain abscess). Occasionally, the pus breaks through the wall of the pleural cavity, either into the lung, or through the wall of the chest (*empyema necessitatis*); in rare instances, there may be perforation into the pericardial cavity, the mediastinum, the esophagus, the trachea, or a large blood vessel.

Diagnosis.—As soon as signs of effusion into the pleural cavity have been discovered, an exploratory puncture should be made, even though one may believe the exudate to be non-purulent. In obscure infections, the possibility of a small empyema should be kept in mind, even in the absence of symptoms referable to the chest; a röntgenogram of the whole chest may reveal an encapsulated effusion, an interlobar, a supradiaphragmatic, or a mediastinal shadow.

In cases of pneumonia and of pulmonary tuberculosis, the possibility of empyema, either as a complication or as a sequel, should be thought of.

When a pleural effusion has been shown to be serofibrinous, it should

be remembered that it may become purulent later, and, also, that a pleuritis may have a serous exudate in one region and a purulent exudate in another.

I have been astonished to find how often diagnosis is delayed through failure to make exploratory puncture with a long needle of wide lumen. It is well to keep a vacuum in the syringe during withdrawal of the needle, and, after withdrawal, to drive any droplet of fluid out of the needle for examination for pus. A single "dry tap" by no means excludes empyema. When negative, repeated puncture at several sites may be necessary before a conclusion that there is no empyema is warranted.

In the **differential diagnosis** from conditions simulating empyema, great difficulties are sometimes encountered. Even the most experienced consultant may at times be at a loss to distinguish a mediastinal empyema from other *mediastinal masses*, a diaphragmatic empyema from a *subphrenic abscess*, an interlobar empyema from a *lung tumor*, or an encapsulated empyema from a *pulmonary abscess extending to the surface of the lung*. If, however, the anamnesis be carefully considered, a thorough general physical examination be made, the leukocytes counted, an exploratory puncture done, and röntgenograms utilized, there should be but few errors, either of omission or commission, made.

iv. Pleurisy with Putrid Exudate

(*Putrid Empyema, Fetid Pleurisy, Ozenous Pleuritis, Gangrenous Empyema*)

Etiology.—The foul odor is due to the presence of putrefactive bacteria; these are nearly always, if not always, anaërobic.

A putrid empyema may follow pulmonary gangrene, putrid bronchitis, or bronchiectasis. Or it may be due to some perforative lesion of the esophagus or to extension from a subphrenic process.

Symptomatology.—The patients deteriorate more rapidly than in nonputrid empyema. They emaciate quickly and look badly; the pulse is small and frequent, there is complete anorexia and the prostration may be extreme.

On exploratory puncture, the punctate yields a putrid odor, and on this the diagnosis depends. Sometimes gas develops. (See Pyopneumothorax).

(c) *Pleural Thickening*

(*Pleuritis chronica productiva*)

Definition.—A chronic inflammation of the pleura with formation of new fibrous tissue and with adhesions between the two layers. The result may be (1) obliteration of a whole pleural cavity on one side with re

of the thorax, (2) partial but extensive obliteration, or (3) circumscribed adhesions.

Etiology.—Delicate pleural adhesions and slight thickening may follow simple pleurisies, but great thickenings are most often due to tuberculous pleurisy.

Symptoms and Signs.—The patients may be slightly cyanotic, and they often show dyspnea on exertion. In obliteration of one pleural cavity with retraction of the thorax (*retrécissement thoracique*), one side of the chest is narrower and shorter than the other, there is scoliosis with concavity toward the shrunken side, the shoulder is lower than its fellow (as is also the nipple), and the intercostal spaces are narrowed. There is diminished expansion, dullness on percussion, and enfeeblement of breath and voice sounds and of vocal fremitus. Litten's phenomenon is absent. As the side becomes shrunken, the mediastinum and the heart are drawn over. If there be much thickening, an exploratory needle meets characteristic resistance and may have to be shoved through a thick layer of tough fibrous tissue before the resistance is overcome (Rosenbach's "palpatory puncture").

On x-ray examination, the whole lung area is darker than normal, the dislocation of the heart and mediastinum is obvious, and the changes in the form of the bony thorax are visible. More circumscribed pleural thickenings may be recognizable as broad shadows or as cords. These may be difficult to distinguish from exudates unless it be remembered that when a pleural thickening is close to the röntgenoscopic screen or the x-ray plate, the shadow is deeper than when the examination is made in the opposite direction, whereas with exudates, the difference does not exist at all or is only very slight.

When a pleural thickening is calcified, remarkable x-ray pictures are obtained (circular or radiating shadows). Adhesions to the diaphragm are often exquisitely demonstrable by the x-ray. A plate exposed on deep inspiration shows the distortion of the upper surface of the diaphragm at the point of adhesion. When patients complain of pain on deep inspiration, especially with change of weather, pleural adhesions should be suspected; even if a röntgenogram be negative, one should insist upon thorough röntgenoscopy in different directions before ruling out pleural adhesions; many supposed simulants have, in reality, adhesions.

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2. Circulatory Disturbances Involving the Pleura

Under this heading are included (a) hydrothorax, (b) hemothorax, and (c) chylothorax.

(*a*) *Hydrothorax*

Definition.—A collection of thin, clear, yellowish fluid, poor in cells, in the pleural cavity—a transudate, not an inflammatory exudate.

Etiology.—Hydrothorax is most often secondary to the general circulatory disturbance of cardiac or renal disease, being a part of a general dropsy or anasarca, but occasionally it is due to local obstructions to the circulation of the blood or lymph from the pressure of tumors or of enlarged mediastinal or bronchopulmonary lymph glands. Often bilateral (as in general anasarca), it may, when due to dilatation of the right heart and pressure upon the azygos vein, be unilateral (usually right-sided), and independent of general hydrops.

Symptoms and Signs.—The fluid obtained by exploratory puncture has the characters of a transudate (specific gravity usually below 1.012, no precipitate with 3 per cent acetic acid in the cold) rather than those of an exudate (specific gravity usually above 1.018). (See Exploratory Punctures.) Fever and pain are usually absent; if present, they are not due to the hydrothorax. Dyspnea is a prominent symptom. The physical signs are those of pleural effusion (*q. v.*). It was formerly believed that shifting dullness may be more marked in hydrothorax than in pleurisy with effusion, but in my experience this has not been so. Small amounts of iodin, or of KI, given by mouth, can, it is said, be demonstrated in transudates but not in exudates.

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(*b*) *Hemothorax*

Definition.—An accumulation of blood in one pleural cavity.

Etiology.—Hemorrhages into the pleural cavity occur from rupture of an aneurism, from erosion of intercostal vessels (tumor, caries of rib), or from trauma; the latter is by far the most common cause and hemothorax is accordingly more often met with in the surgical than in the medical wards.

Hemothorax is to be distinguished from a hemorrhagic pleuritic effusion, which, as has already been pointed out, most often points to a tuberculous pleuritis, occasionally to a carcinoma, now and then to a pyogenic pleuritis (pneumococcus), or to a hemorrhagic diathesis.

Symptomatology.—In addition to the ordinary signs of a rapidly developing effusion, pressure symptoms may appear, with increasing dyspnea and dislocation of the heart and of the mediastinum. There are also signs of anemia due to internal hemorrhage (pallor, tachycardia, sweating, syncope); fever is usually present after the first or second day. The physical signs are, of course, like those of pleural effusion, but an exploratory puncture reveals blood, and it is interesting that the blood shows, as a rule, no tendency to coagulate, owing, perhaps, to a change that fibrinogen undergoes when it comes into contact with the endothelial covering of the pleura.

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(*c*) *Chylothorax*

Definition.—An accumulation of a milky fluid in the pleura The fluid may consist of pure chyle (*chylothorax proper*), or of or serofibrinous fluid containing fat droplets not derived from tl channels (*pseudochylous effusion*).

Etiology.—Chylothorax proper depends upon a break in the c of the thoracic duct with escape of its chyle; the lesion may

trauma, to carcinoma of the pleura, to thrombosis of the left subclavian vein, to compression of the thoracic duct by tumors or enlarged glands, or to blocking of the duct by a parasite.

Pseudochylous effusions are pleural exudates (due usually either to tuberculosis or to carcinoma) in which the fluid becomes milky owing to the escape of fat droplets from the disintegrating cells (endothelium, leukocytes).

Symptomatology.—The physical signs are those of a pleural effusion. On exploratory puncture, the milkiness of the fluid indicates either a chylous or a pseudochylous nature. Microscopic examination usually quickly differentiates between the two, since in chylous effusions cells are absent and the fat droplets are minute and equal in size, while in pseudochylous effusions many cells undergoing fatty degeneration are present and the free fat droplets vary in size.

If the fat be extracted, it will be found to be present in large amounts (up to 10 per cent) in true chylothorax, and in only small amounts (rarely over 0.5 per cent) in pseudochylous effusions; this explains why, when allowed to stand, a thick cream rises on the surface of a chylous effusion, whereas only a thinner layer will form upon a pseudochylous fluid.

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3. Gas in the Pleural Cavity; Pneumothorax

Under this heading, we have to consider three conditions: (1) *pure pneumothorax,* in which there is gas only in the pleural cavity; (2) *seropneumothorax,* in which besides the gas there is serous fluid due to a complicating pleuritis serosa; and (3) *pyopneumothorax,* in which besides the gas there is pus, due to an associated pleuritis purulenta.

When the gas enters through the external wall of the chest, for example, after a pleural tapping, or during a surgical operation for resection of a rib, we speak of an *external* pneumothorax; when the gas enters the pleural cavity from the lung itself, or is formed in the pleural cavity as a result of putrefaction, we speak of an *internal* pneumothorax. When the perforation in the wall of the pleural cavity is patent during both inspiration and expiration, we speak of an *open* pneumothorax; if the opening become closed after its formation, so as to be patent neither during

inspiration nor expiration, we speak of a *closed* pneumothorax; and when the perforation is patent during inspiration but is wholly or partially closed during expiration, as is commonly the case in spontaneous pneumothorax, we speak of a *valvular* pneumothorax (see below).

Etiology.—From 80 to 90 per cent of all cases of pneumothorax are due to pulmonary tuberculosis, the rupture of the lung in this disease occurring about four times as often in men as in women. In the remaining 10-20 per cent of the cases, pulmonary gangrene, empyema pleurae, trauma, pulmonary abscess, bronchiectasis and pulmonary emphysema are most often responsible. Among the conditions that may more rarely be complicated by pneumothorax may be mentioned thoracentesis, pulmonary infarction, perforating ulcer of the stomach or esophagus, echinococcus invasion, subphrenic abscess, and caries of a rib or of the sternum.

Since the method of treating pulmonary tuberculosis by injecting air or nitrogen into the pleural cavity (artificial pneumothorax) has come into vogue, much new light has been thrown upon the pathological physiology of pneumothorax by clinical and experimental study.

In spontaneous (internal) pneumothorax, the perforation of the lung most commonly occurs in the lower part of the upper lobe; at autopsy, the perforation is usually found in an area between the mammillary and the axillary line at a level between the second and the fourth rib.

In seropneumothorax, the pleuritis is due to bacterial infection; in pyopneumothorax, putrefactive (anaërobic) as well as pyogenic (aërobic) bacteria are present.

Symptomatology.—Pneumothorax usually occurs suddenly, with pain, dyspnea, and feeling of constriction; there is often collapse with marked cyanosis. In the stormiest type, death may occur in a few hours or even in a few minutes from asphyxia. More often, however, the phenomena are less severe; the patient feels some pain in his chest and notices that he has become short of breath without apparent cause. In a few instances, the occurrence of pneumothorax has caused no symptoms recognized by the phthisical patient, and the physician has found the signs of it on making one of his regular routine examinations.

When air enters the pleural cavity, there is sudden retraction of the lung to the region of the hilus, exquisitely demonstrable by the x-ray. The heart and the whole mediastinum are drawn over to the healthy side where the pleura is still under negative pressure.

In open pneumothorax (rarely seen) the internal pressure is
external pressure; respiration is ineffective and death from asphyx
In closed pneumothorax, the internal pressure increases as soon
matory exudate develops; here there is less danger of asphyxia but
as in exudative pleuritis, of circulatory disturbances. In so-c
pneumothorax (the commonest form), air enters the pleural cavity
but cannot get out during expiration; this may lead to extreme dis
dangerous interference with the circulation.

On *physical examination,* the affected side is usually distended and immobile, or nearly immobile, on respiration. Litten's phenomenon is absent on the affected side. The apex beat of the heart is displaced toward the normal side. Vocal fremitus is absent or greatly enfeebled on the side of the pneumothorax. When the mediastinal tissues are markedly dislocated, the larynx and trachea may also be palpably displaced in the same direction. On percussion over the pneumothorax, there is usually hyperresonance, often tympanitic or amphoric in quality; the percussion note varies, however, markedly, according to the tension of the gas in the pleural cavity; there may occasionally be actual dullness! The coin sound (*bruit d'airain*) is very characteristic; thus on listening at the back of the chest, while an assistant taps one coin on another in front, a distinct, metallic, echoing sound is heard. A similar metallic sound can be heard if one taps on a plexímeter with the end of a lead pencil or with the handle of a percussion hammer. The sound is sometimes elicitable only when certain circumscribed areas are thus percussed.

If fluid or pus be present (seropneumothorax, pyopneumothorax) there is dullness bounded by a *horizontal* line above, and the dullness shifting on any change of posture is found still to be horizontal, in contradistinction to what happens in simple pleural effusions without pneumothorax. On shaking the patient, a metallic splashing sound may be audible (Hippocratic succussion splash). Sometimes the sound can be heard at some distance; a patient may hear such a sound himself, and voluntarily produce it by shaking his trunk, to the astonishment of bystanders. In such cases, too, the metallic sound of a falling drop (*gutta cadens*) may be audible. When the lung fistula is patent and lies below the surface of the fluid in the pleural cavity, a gurgling sound like that due to gas bubbles passing through fluid may be heard; this is the so-called "water-whistle" sound, or "fistular murmur."

On auscultation over a pneumothorax the breath sounds are usually markedly enfeebled or entirely suppressed. In some cases, loud amphoric breathing may be audible.

If pneumothorax be suspected, an x-ray examination should, if possible, be made. The findings in the lung areas in complete unilateral pneumothorax are very characteristic. There is abnormal clearness on the affected side; the normal lung markings are absent; the lung is retracted to its root. The diaphragm stands low, though it may be normally curved. The displacement of the cardiovascular stripe is striking. The horizontal level of any fluid present is clearly visible. On Hippocratic succussion, waves in the fluid may be röntgenoscopically observed. On röntgenoscopy, too, a so-called "paradoxical movement of the diaphragm" may be visible, the diaphragmatic shadow moving upward on inspiration and downward on expiration on the affected side; since the opposite occurs on the normal

side a peculiar "teeterlike" or "see-saw" movement of the two halves of the diaphragm is observable.

In the artificial pneumothorax used in the treatment of chronic pulmonary tuberculosis, retraction of the lung may be only partial, owing to

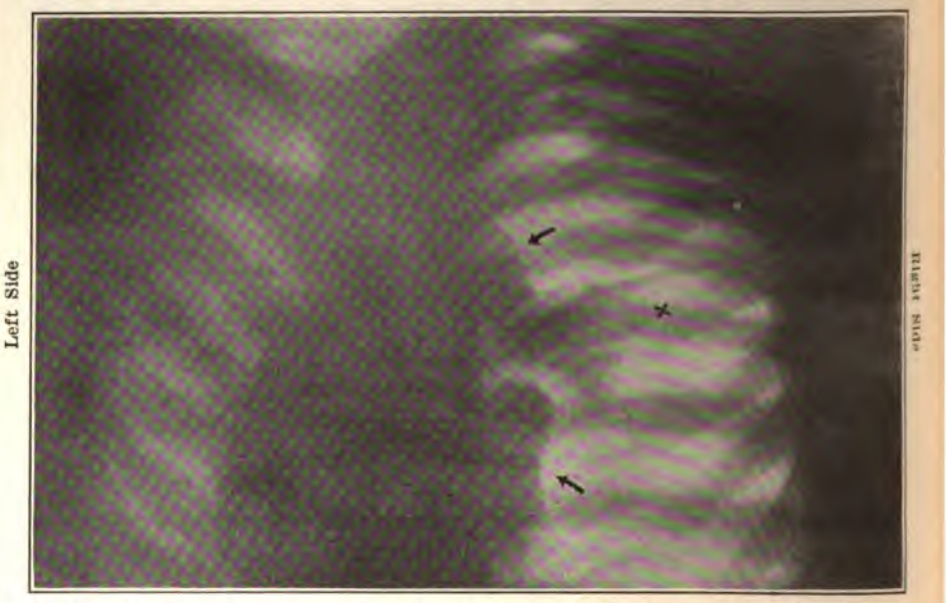

Fig. 180.—Artificial Pneumothorax with Pleural Adhesions. The Arrows Indicate the Margin of the Collapsed Lung; the Cross Shows the Portion of the Lung Held by Pleural Adhesions. (X-ray Dept., J. H. H.)

pleural adhesions. Spontaneous partial pneumothorax is not an uncommon finding in röntgenograms of phthisical lungs.

Diagnosis.—The recognition of PURE PNEUMOTHORAX is, as a rule, not difficult if the possibility of its existence be thought of. Too often, unless dyspnea have come on suddenly, the physician fails to suspect it. This fact emphasizes again the importance of thorough physical examination of the chest in every dyspneic patient. The physical signs are usually characteristic enough if the physician systematically studies them. A lagging side on respiration, with diminished vocal fremitus and enfeebled or suppressed breath sounds, even without much change in the note on percussion, should always arouse suspicion and lead the examiner to test the coin sound, to look for the displacement of organs, and to study a röntgenogram of the chest.

In the DIFFERENTIAL DIAGNOSIS, we must distinguish total unilateral pneumothorax (1) from unilateral *emphysema* (coin-test negative, x-ray decisive); we must distinguish partial pneumothorax (2) from *diaphragmatic hernia* (anamnesis, auscultation, röntgenogram); (3) from *gaseous distention of stomach* (passage of stomach tube, x-ray); and (4) from an

intrapulmonary cavity; in the last instance, a röntgenogram may be inconclusive, but the onset of pneumothorax is usually sudden, and the intercostal spaces opposite it bulge, whereas an intrapulmonary cavity develops slowly and there is often retraction of the intercostal spaces over it (Staehelin).

In SEROPNEUMOTHORAX the diagnosis is very easy if Hippocratic succussion be practiced, and if the x-ray reveal the presence of fluid with horizontal level below the gas. To distinguish it from pyopneumothorax, exploratory puncture should be made below the level of the surface of the fluid. Should pus be found, a careful bacterio-diagnostic study should follow, since the therapy of tuberculous pyopneumothorax differs from that of non-tuberculous forms. Even in the tuberculous form, the possibility of a mixed infection should not be forgotten. Occasionally, an artificial pure pneumothorax of phthisicotherapeutic origin may be converted into a PYOPNEUMOTHORAX through secondary infection, or through the rupture of a tuberculous cavity into it. When the pus of a pyopneumothorax is putrid, anaërobic bacilli will usually be demonstrable in it.

Subphrenic pyopneumothorax may clinically resemble a partial superphrenic pyopneumothorax. It is due to the collection of gas below the diaphragm in gaseous subphrenic abscesses, or to rupture of the stomach or of the lower end of the esophagus in cancer. Here the x-ray plate will differentiate, since in the subphrenic cases the cavity will be bounded above by the shadow of the diaphragm (pushed up into the thorax); moreover, Litten's sign may still be present, and, sometimes, the punctate has a feculent odor.

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4. Tumors of the Pleura

Primary tumors of the pleura are rare (endothelial cancer; sar
ondary tumors are much more common, especially metastases from
breast, lungs, stomach, esophagus, or thymus. In secondary cancer
the membrane is often studded over with nodules, which at autop
of tubercles; the condition is known as *carcinosis pleurae.*

Cancer of the pleura usually develops with the signs of pleur
malignant nature may be first suspected from the bloody character
the presence of cancer cells in it, the resistance of the "pleuritis"

ment, the enlargement of glands above the clavicle and in the axilla, the development of cachexia, or the persistence of an intercostal neuralgia.

Tumors of the pleura must be distinguished from carcinoma or lymphosarcoma of the lung (*q. v.*) and from mediastinal masses (sarcoma, aneurism, echinococcus, esophageal carcinoma). X-ray examinations may help in the differentiation.

I have now under observation a man aged 39, referred to me for study by Dr. A. D. Parrott of Kinston, N. C., who for more than a year has suffered from pain in the back and right side of the chest. The pain begins in the right hypochondrium and radiates into the back. This pain is often so severe as to prevent sleep. Its location led a very good surgeon to explore the gall-bladder region. Some adhesions were found between the gall-bladder and the liver and these were severed, but without relief to the pain. Later the pain radiated also into the region of the right scapula and into the right side of the neck. Returning to his surgeon, x-rays were made of the kidney regions and a small shadow was found in the röntgenogram of the left kidney. A stone was removed, but without relief to the pain. A few months before consulting me the patient began to have outspoken dyspnea and a dry cough, and retraction of the right thorax became noticeable. On physical examination, I found retraction of the whole right side of the chest and outspoken dullness in the lower half of the chest, with flatness at the base. In the hospital over a liter of fluid was drawn off. This fluid was turbid and contained a large number of endothelial cells rich in fat droplets. No tubercle bacilli were present. A röntgenogram revealed a mass in the lower right pleura. There can be but little doubt that we are dealing here with a primary tumor of the pleura—so-called pleural endothelioma or pleural cancer.

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5. Parasites of the Pleura

The most common parasite to invade the pleural cavity is echinococcus. A good many cases are reported in the literature under the name hydatid of the pleura. Such echinococcus cysts may be mistaken for tumors or cysts of the liver.

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G. Diagnosis of the Principal Diseases of the Mediastinum

The mediastinum subserves three main functions:

It is a *septum* between the two lungs, making each lung and pleural cavity independent of the other, so that the intrathoracic pressure may under pathological conditions differ on one side from that on the other. This septum may be displaced lateralward as a whole, or at either one of its two weak spots. One weak spot in the septum is situated in the anterior part of the upper mediastinum in the region of the thymus fat (Nitsch). Here the mediastinum is often reduced to a thin membrane consisting of the adherent layers of the mediastinal pleura. If one pleural cavity be blown up in the cadaver, this weak spot of the mediastinal septum will balloon out into the opposite half of the thorax.

Another weak spot in the mediastinal septum lies in the posterior part of the inferior mediastinum. It is bounded in front by the esophagus and the heart, and behind by the spine and aorta. Here, ag cadaver, inflation of one pleural cavity leads to ballooning o second weak spot of the septum into the opposite half of t (Nitsch). This weak spot has, however, nothing to do with the the paravertebral triangle of dullness in pleural effusion (*q.*

The second main function of the mediastinum is to serve *lodging important channels of communication* (heart and g

trachea and larger bronchi, esophagus, nerve trunks, including the N. vagus, N. sympathicus, N. phrenicus, and Nn. intercostales).

The third main function of the mediastinum is to serve as an important *area of the lymphatic system* (ductus thoracicus, mediastinal lymph glands, lymph spaces of mediastinal connective tissue communicating with the peritoneum below). The lymph spaces in the mediastinum are often the site of inflammatory processes (acute and chronic mediastinitis), and the lymph glands here are frequently the site of important pathological changes (tuberculosis, Hodgkin's disease, lymphosarcoma). Since the advent of röntgenographic methods a flood of new light has been thrown upon these pathological processes that involve the mediastinal lymph glands and lymph spaces.

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Classification of Diseases of the Mediastinum

The most convenient classification at present is that suggested by G. von Bergmann:

1. Displacement of the mediastinum through pressure or traction from the outside (disturbances of the septal function).
   (a) Total displacements.
   (b) Partial displacements.

2. Space-occupying processes in the mediastinum (disturbances of the channels of communication in the mediastinum).
   (a) Small masses.
   (b) Large masses.

3. Diseases involving the lymph spaces of the mediastinum (disturbances of the lymphatic function).
   (a) Acute mediastinitis.
   (b) Chronic mediastinitis.
   (c) Mediastinal hemorrhage.
   (d) Mediastinal emphysema.

Diseases of the heart, of the pericardium, of the esophagus, of the aorta, etc., though strictly speaking they belong to the mediastinum, are considered elsewhere.

1. Displacements of the Mediastinum Through Pressure or Traction

(*a*) *Total Displacements*

The mediastinum is more or less movable and distensible. At every breath the distance between the sternum and the spine is increased during inspiration and diminished during expiration. Again, changes in the pressure in each half of the thorax can lead to concavity or convexity of the mediastinum toward the opposite side, according as a negative or positive pressure is greater in one half of the thorax than in the other (pleural effusion, pneumothorax, bronchiostenosis). The degree of displacement is also affected by the degree of rigidity of the mediastinal septum, which varies much in different persons; in chronic mediastinitis the septum may become quite rigid.

The septum is less often pressed over to the opposite side by an exudate or by a pneumothorax than drawn over by the negative pressure of the actively-breathing half of the thorax (Brauer).

Chronic cicatricial processes (pleuromediastinitis, pleuropericarditis externa) may pull the mediastinum far to one side. Such a process on the right may pull the heart far to the right, simulating the dextrocardia of situs inversus.

(*b*) *Partial Displacements*

The two weak spots of the mediastinum have been described above; in pneumothorax they may balloon out into the opposite side (Brauer), and in pleuritis they may bulge into the healthy side like a mediastinal hernia (Spengler). Such partial displacements can be recognized by röntgenography and sometimes by percussion. In cicatricial contraction of one lung there may be a dislocation of a "weak spot" toward the diseased side.

2. Space-occupying Processes in the Mediastinum

Symptoms.—Certain symptoms are common to pathological processes that occupy space in the mediastinum (tumors, hemorrhages, abscesses, mediastinal pneumothorax, mediastinal emphysema, aneurisms, esophageal diverticula, enlarged lymph glands). These symptoms arise chiefly from the compression of structures in the mediastinum (veins, a passages, esophagus, nerves).

Two types of collateral venous circulation are met with in r disease. In the first type there is general dilatation of the sma veins over the whole chest, back and upper abdomen. On pr such dilated veins, one finds that they swell above the point of and collapse below it, indicating that the current is flowing fro

cava superior to the vena cava inferior. This is the condition seen when the collateral circulation is fairly sufficient. In the second type the dilated veins may not be easily visible, but, instead, there is a general cyanosis of the skin of the upper half of the body, with pitting on pressure and obliteration of the normal contours of the neck and thorax, the swelling extending downward as far as the level of the diaphragm. This second type is known as the "collar of Stokes."

Fig. 181.—Collateral Circulation Between the Superior and the Inferior Vena Cava in a Case of Mediastinal Tumor. (By courtesy of Dr. Rowntree.)

Sometimes one sees a unilateral edema due to compression or thrombosis of one innominate vein. The varying clinical picture, according to the number of veins involved in the compression (superior cava, innominates, V. azygos, V. hemiazygos, Vv. pulmonales), has been described by Dieulafoy. In case the V. azygos is free when the superior cava is compressed distal from it, the collateral circulation is carried on not only by the inferior cava, but also through the V. azygos, in which event there is less dilatation of the cutaneous veins. According to the degree of insufficiency of compensation by collateral circulation one sees every transition from a normal skin with dilated veins, through moderate turgor and definite edema, to the most marked edema that stretches the skin and makes it shiny. Along with this edema of the upper half of the body, one sees also in the marked cases deep cyanosis of the lips and face, and injection of the conjunctival vessels; such patients suffer from headaches and vertigo, and often from severe epistaxis. Blood counts from blood drawn from the upper half of the body may show an outspoken polyglobulia, while a count made from blood from the toe may be normal.

A unilateral hydrothorax may be due to compression of the V. azygos or the V. hemiazygos alone; when the thoracic duct is also pressed upon, the fluid of the hydrothorax becomes chylous.

Compression of the aorta or of the pulmonary artery in the mediastinum may give rise to a systolic stenosis-murmur. Should the aorta be compressed at the site of origin of the innominate artery or of the left subclavian artery, the pulse at one wrist may be feebler than that at the other (pulsus differens).

When the air passages are compressed by masses in the mediastinum,

important diagnostic symptoms may arise; thus in compression of the trachea the signs of tracheal stenosis appear (difficult breathing, audible stridor, retraction of the thorax). When one main bronchus is compressed there is tachypnea, lessened expansion, enfeebled breath sounds, and enfeebled vocal fremitus on the affected side. The percussion note may remain clear. Sometimes stenosis murmurs may become audible.

If the lung itself be compressed, the physical signs vary according to the site of the compression; usually the breath sounds are enfeebled, but sometimes bronchial breathing is transmitted through the mass, especially in the interscapular region.

If the esophagus be compressed, the patient will complain of dysphagia and localized pain. Examination with the esophageal bougie, or, better, röntgenography with the aid of thick bismuth paste, will show the site and extent of the esophageal stenosis. Esophagoscopy may also be resorted to.

When the nerves of the mediastinum are compressed, important diagnostic signs also arise; thus, compression of the N. vagus and especially of its branch, the N. recurrens, gives rise first to posticus paralysis of the larynx. When the lesion is unilateral, there may be no hoarseness, but laryngoscopy will reveal the paralysis. The irritable cough of bronchial-gland tuberculosis and the brassy cough of aortic aneurism are to be regarded as pressure symptoms from mediastinal involvement of the N. vagus. Other symptoms due to pressure on the N. vagus include bradycardia when the nerve is merely irritated, and tachycardia when it is sufficiently compressed to be paralyzed. Nausea, vomiting, hyperacidity and disturbance of intestinal function may also follow vagal injury in the mediastinum.

Involvement of the N. sympathicus may cause protrusio bulbi (unilateral or bilateral), anisocoria, unilateral hyperhidrosis or anhidrosis, sympathetic ptosis, etc.

Compression of the N. phrenicus may cause hiccough or may give rise to inequality of contraction of the two halves of the diaphragm (röntgenoscopy); one should make sure, however, that such inequality does not depend upon unilateral bronchostenosis or upon phrenic involvement through apical tuberculosis rather than upon mediastinal compression.

Pressure on the Nn. intercostales may cause severe intercostal neuralgia.

Other physical signs of space-occupying processes in the mediastinum include (1) dislocation of the heart and of the lungs, and (2) distention of the thoracic wall. These effects are recognizable by careful examination of the thorax.

After determining the existence of symptoms pointing to a space-occupying process in the mediastinum, it is necessary to try to determine the nature of that process. This part of the problem has been rendered

easier since the introduction of röntgenographic methods in intrathoracic diagnosis.

(*a*) *Röntgenography of the Mediastinum*

By means of x-rays we can determine the position and size of any space-occupying mass or masses in the mediastinum. In general, röntgenography is here more helpful than röntgenoscopy, but for the study of pulsating masses (aneurisms, pulsating tumors, pulsating empyemas) röntgenoscopy is essential.

In the diagnosis of large tumors of the mediastinum, several types can be distinguished in x-ray pictures; thus, if in the röntgenogram one sees a shadow projecting like a mole-hill at the junction between the cardiovascular stripe and the clear lung area, its surface being either hemispherical, with the center of the sphere lying at the root of the lung, or uneven, with jagged contours, one can be sure that he is dealing with a hilus tumor. Such a mediastinal tumor at the hilus has to be distinguished from a tumor of the lung on the one hand and from an aortic aneurism on the other.

In large tumors of the mediastinum due to Hodgkin's disease, one sees a mass either to the right or to the left of the sternum, or on both sides, usually feebly convex, and extending all the way from the clavicle down to the heart. When the tumor projects to the left side, the differential diagnosis from aortic aneurism may be difficult, though the pulsation in aneurism, visible on röntgenoscopy, may help. Tumors of the lung itself are usually easily distinguishable from mediastinal tumors proper, though in some cases the röntgenogram leaves one uncertain. Thus, a tumor arising in a lymph gland at the hilus of the lung, or in the bronchial mucous membrane near the hilus, usually gives rise to a shadow extending out into the lung but more or less separable from the cardiovascular stripe; and when the shadow becomes confused with the cardiovascular stripe, the predominant involvement of one lobe of a lung may give one the clew to a pulmonary rather than a mediastinal origin of the mass (v. Bergmann).

In judging of the nature of mediastinal tumors, one should pay attention not only to the appearance of the main shadow, but also to certain additional points: (1) the presence or absence of a pleural effusion, (2) the presence or absence of darkening of one whole lung area (bronchiostenosis), (3) the involvement or non-involvement of the arch of the aorta. It is also important to make out, if possible, whether we are dealing with a compact uniform mass or with a composite mass made up of several parts, as in lymph-gland enlargement (bronchial-gland tuberculosis, Hodgkin's disease). Examinations with the aid of the x-ray have proven so helpful in the differential diagnosis of mediastinal growths that students and physicians sometimes fail to apply thoroughly, in addition, the ordinary

physical methods of examination. This is a serious error, for the diagnostician who intelligently utilizes all the methods available in diagnosis will make fewer mistakes than he who relies upon a more limited application of diagnostic technic. When applying Röntgen rays to intrathoracic diagnosis the röntgenographer should not be satisfied with röntgenoscopy alone, nor with röntgenography alone; he should use both methods, and in some cases may find it necessary to make his observations not only in the anteroposterior direction but also in the transverse and oblique diameters of the chest. For wider reading on this subject, see Christian's article in Osler and McCrae's "Modern Medicine," von Bergmann's article in Mohr

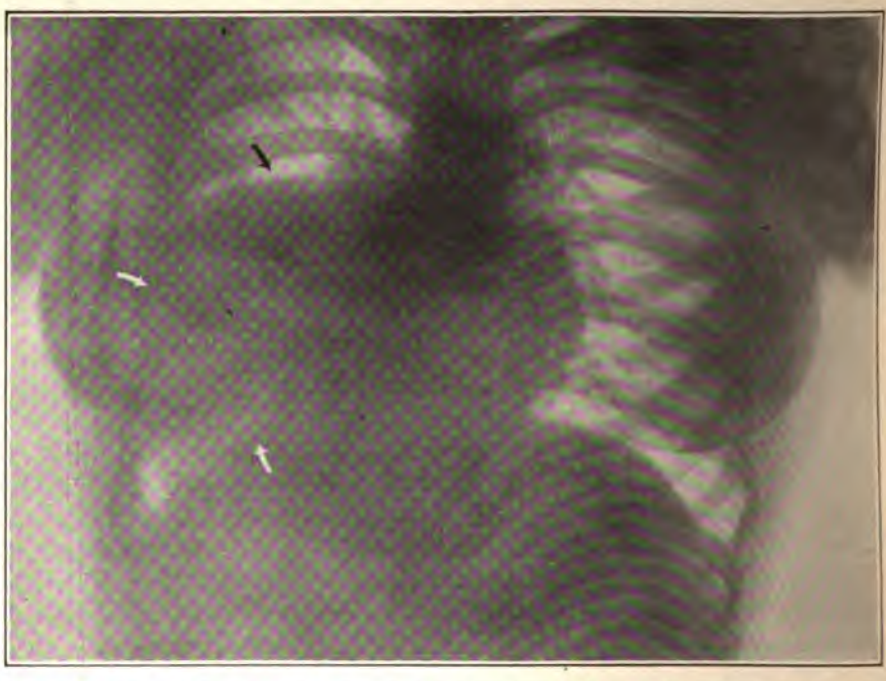

Fig. 182.—Large Vascular Sarcoma of Posterior Mediastinum. Clinically, a Pulsation Was Visible Over a Dull Area in the Lower Back. The Shadow of the Tumor Is Not to be Confused with the Shadow Due to the Mammary Gland. (X-ray Dept., J. H. H.)

and Staehelin, Dieulafoy's paper, and the Atlases of Holtzknecht and of Rieder and Rosenthal.

In the differential diagnosis between aneurism of the aorta and malignant tumors of the mediastinum the following points are worthy of emphasis: If the normal form and position of the arch of the aorta can be seen undisturbed by the suspected mass, it is almost certain that we deal with aneurism. On the other hand, a dislocated aorta does not necessarily mean aneurism, since tumors can also cause displacements. Expansile pulsation, when definitely recognizable, is helpful in

the diagnosis of aneurism, but some aneurisms pulsate but little, and some mediastinal tumors show a propagated pulsation which may be difficult to distinguish from aneurism. If the whole physical examination be carefully made, and the x-ray findings be thoroughly analyzed and judged, the results of these, together with the general clinical considerations of the case (Wassermann reaction!), will rarely leave one in doubt.

Dislocation of the upper anterior weak spot of the mediastinum to one side, visible on röntgenoscopy, is sometimes helpful in diagnosis. It is to be remembered that in bronchiostenosis the bulging is toward the side of the stenosis, as the weak spot of the mediastinum is drawn over to the diseased side, while in pleural effusion and in pneumothorax exactly the opposite occurs, in that the mediastinum is drawn over toward the healthy side, owing to the greater negative pressure on inspiration on that side.

On röntgenography of the thorax we may discover changes in the mediastinum that often have given rise to no symptoms and have therefore been unsuspected (enlargement of mediastinal or of bronchial lymph glands, beginning aneurism of the aorta, esophageal carcinoma, tumor in the region of the sternoclavicular joint).

The frequency of mediastinitis in röntgenograms of the thorax is now known to every clinician familiar with this technic. Occasionally, a mediastinal emphysema or a mediastinal pneumothorax can be recognized in a röntgenogram (v. Bergmann).

(*b*) *Varieties of Mediastinal Tumors*

Among the masses originating in the mediastinum itself, exclusive of extramediastinal processes, intramediastinal suppurations, hemorrhages and emphysema, and of enlargements of the esophagus, heart, pericardium and great vessels, we may consider two groups: (1) small mediastinal masses, and (2) large mediastinal masses. The *smaller mediastinal masses* originate chiefly in the lymph glands; they include tuberculous glands, especially the tuberculous bronchial glands of children, syphilitic lymph glands, the enlarged lymph glands in Hodgkin's disease and in leukemia, as well as enlargements due to acute or chronic lymphadenitis or to metastatic tumor-growth.

The *large mediastinal tumors* arise also chiefly from lymph glands or from the thymus. Among the larger mediastinal tumors originating in lymph glands may be included: (1) Hodgkin's disease, (2) lymphosarcoma, (3) leukemic and aleukemic lymphadenosis, (4) metastatic sarcomata or carcinomata. Those arising in the thymus usually take the form of the so-called thymus-sarcoma, sometimes called thymus-carcinoma.

Certain benign tumors of the mediastinum (teratoma, dermoid cyst, echinococcus cyst, intrathoracic goiter) may occasionally be met with. In one tumor personally observed, the mass disappeared entirely, as

demonstrated by röntgenograms, after radium treatment by Drs. Kelly and Burnam.

(c) *Diagnosis of Mediastinal Tumors*

If the symptomatology above described be thoroughly mastered, a correct diagnosis should be arrived at in the majority of cases. Pressure symptoms are usually the first to give a clew, though a mediastinal tumor is sometimes treated for a considerable period as something else (angina pectoris, pulmonary tuberculosis, chronic bronchitis, laryngitis, bronchial asthma, whooping-cough), before the true nature of the process is recognized. If on inspection and palpation there be no collateral circulation, edema, abnormal pulsation, or bulging of the chest wall, on percussion no abnormal dullness, and on x-ray examination in both the dorsoventral and in the oblique diameter no shadow visible, certainly no large mediastinal mass can be present.

It should be kept in mind that pressure symptoms involving the great vessels (collateral circulation, edema) point rather to masses in the anterior mediastinum, whereas pressure upon the esophagus (dysphagia), or upon the air passages (dyspnea, bronchiostenosis), points rather to the posterior mediastinum.

Benign processes in the mediastinum are much rarer than the more serious involvements. Malignant masses usually enlarge rapidly and the general state of the patient quickly becomes impaired.

The general condition of the lymph glands is very important in differential diagnosis. If a mediastinal mass coexists with enlargement of the lymph glands in the neck, one of the latter may be excised for histological diagnosis. I have repeatedly been able by means of such gland excisions to recognize the sarcomatous or malignant lymphomatous nature of a mediastinal tumor. A thorough blood examination, including a careful differential count of the white corpuscles, should always be made. A true leukemia would then never be overlooked, and, if Bunting is right, the diagnosis of Hodgkin's disease can, in many cases at least, be made early from the blood picture.

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3. Diseases Involving the Lymph Spaces of the Mediastinum

Here we consider the processes that develop in the mediastinal tissues themselves. These may be the seat either of acute inflammatory processes (mediastinitis acuta), or of chronic inflammation (mediastinitis chronica); blood may be diffused through the mediastinal tissues (mediastinal hemorrhage), or these tissues may be infiltrated with air (mediastinal emphysema).

(*a*) *Acute Mediastinitis and Mediastinal Abscess*

Definition.—An acute inflammation, usually involving the anterior mediastinum, more often diffuse than circumscribed, and in many cases leading to suppuration with abscess formation.

Etiology.—In most cases the mediastinitis is due to an infection *per contiguitatem* (neck, larynx, trachea, thyroid, sheath of the carotid artery or jugular vein), most often as an extension from a retropharyngeal abscess following upon suppuration of retropharyngeal lymph glands, tonsillar and peritonsillar abscesses, or suppurative laryngeal perichondritis. Occasionally a mediastinal abscess results from rupture of a pleural empyema, from an abscess of the lung, or a suppurative osteomyelitis. Now and then rupture of the esophagus (carcinoma, foreign body, passage of a bougie), of the trachea, of a pyopericardium, or of a suppurating bronchial gland may be responsible.

Metastatic abscesses occasionally occur in pyemia, in typhoid fever, and in erysipelas. Direct trauma is, in rare instances, an etiological factor.

Symptoms.—Fever and other signs of a severe infection (chills, sweats, loss of weight) develop. The patient complains of pain behind or alongside of the sternum, radiating to both sides. This pain may at first be taken to be stenocardiac in nature. Pressure upon the sternum or upon the chest wall near the sternum increases the pain. In the rare cases in which the posterior mediastinum is involved, the pain may be referred to the spine or to the shoulder blades, or there may be severe intercostal neuralgias. Circumscribed edema of the skin may be present. Pressure symptoms may occur but are less marked than in solid mediastinal tumors; among these, cyanosis, respiratory irregularity of the pulse, and paralysis of the diaphragm are perhaps the most common. There is dulln the sternum, and if an abscess be present its size and positi accurately determined by röntgenography. Sometimes an ab which the mediastinal abscess has originated can be recognize scess may finally perforate the chest wall through one of the spaces, or it may point in the jugulum, or in one of the sup fossae. Unfortunately, mediastinal abscess more often pe

trachea (death from asphyxia), the esophagus, the pericardium, or into the pleural cavity.

(*b*) *Chronic Mediastinitis*

Definition.—A chronic productive inflammation of the mediastinal tissues, leading to fibrous thickening of these tissues, usually arising by extension of a chronic pleurisy (pleuromediastinitis), or, more often still, of a chronic pericarditis (mediastinopericarditis).

Etiology.—The disease may be of tuberculous, of rheumatic, or of unknown origin. It is common in association with the different forms of polyserositis.

Symptoms.—In subacute cases there may be fever and pain, but in the chronic cases these may be entirely absent.

As a result of the fibrosis there is often interference with respiration, owing to the fact that the mediastinum cannot be stretched in the sagittal direction during inspiration. Nerves, arteries and veins may become compressed in the fibrous tissue. On röntgenography the hilus shadows and the pericardial shadows may be markedly deepened.

One of the most important symptoms is the so-called pulsus paradoxus (Griesinger), the pulse becoming smaller or intermitting during deep inspiration; there is at the same time an inspiratory swelling of the large veins of the neck. According to Gaisboeck, the pulsus paradoxus in mediastinitis is to be looked upon as a vascular reflex due to excitation of the vasomotor center from change in the distribution of the blood causing a vasoconstriction at the periphery. Others maintain that the intermission of the pulse is mechanical, due to narrowing of the aorta and other large arteries by the scar tissue during inspiration.

(*c*) *Mediastinal Hemorrhage*

This is most often due to perforation of an aneurism of the aorta or of one of its branches. The condition is rarely recognized during life.

(*d*) *Mediastinal Emphysema*

Since the artificial-pneumothorax therapy of pulmonary tuberculosis has come into vogue, the subject of mediastinal emphysema has assumed a new clinical importance. In connection with pneumothorax therapy it is not uncommon to meet with a *false mediastinal emphysema,* properly known as *subfascial emphysema.* If, for example, in the pneumothorax therapy the cannula is inserted between the intrathoracal fascia lining the intercostal muscles and the ribs on the one side and the costal pleura on the other, the air becomes diffused between these two layers into the loose connective tissue of the endothoracic fascia, causing pain. The air in this

case stays behind the ribs, while in subcutaneous emphysema and in true mediastinal emphysema it appears in the jugulum and spreads out into the skin. In *true mediastinal emphysema,* the air gets into the mediastinal tissue from the larynx, trachea or bronchi, or it may reach the mediastinum from the hilus of the lung, owing to tear of the lung tissue or of one of the small bronchi, or to the perforation of a lung cavity, of a lung abscess, or of a softened tumor.

One's attention may be first called to it by the appearance of subcutaneous emphysema in the neck. On examination the percussion note will be found to be of high pitch and tympanitic over the mediastinum. The heart dullness may be obliterated. On auscultation, crepitation synchronous with the heart's action may be audible. The heart sounds are distant, or may be entirely inaudible. If the pressure be great the dyspnea will be marked.

Not infrequently, owing to the cause of the mediastinal emphysema, a phlegmonous mediastinitis secondarily develops.

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Part VI

Diagnosis of Diseases of the Circulatory Apparatus

(CLINICAL ANGIOLOGY)

SECTION I

METHODS OF DETERMINING THE CONDITION OF THE CIRCULATORY SYSTEM

A. Introduction

The **circulatory apparatus** includes (1) the *heart*, made up of the right atrium, the right ventricle, the left atrium and the left ventricle; (2) the *arteries*, including the pulmonary artery, the aorta, and all their branches; (3) the *veins* of both the pulmonary and the general circulation; (4) the *capillaries;* and (5) *the lymphatic system*, including the lymphatic vessels, the thoracic duct, the lymph glands, and the lymphatic plexuses.

Before taking up the study of diseases of the circulatory system, the anatomy and physiology of this system should be thoroughly mastered, and the physical conditions of the organs in normal circumstances should be well known. A student approaching the study of clinical angiology will, therefore, do well to review the general topographical anatomy of the heart and great vessels, and the form of the heart and its several chambers as seen in fresh specimens, at autopsy, and in formalinized specimens. Anatomical and histological atlases and texts should be consulted, and the study should include the microscopic anatomy and histology of the heart muscle, the distribution of the coronary arteries and of the cardiac nerves, the structure of the larger and smaller arteries, of the larger and smaller veins, of the capillaries, and of the lymphatics.

The older and the newer physiology of the heart and of the circulation should also be carefully reviewed. It is necessary to know how the heart does its work. The general mechanics of the circulation should be well understood, including the effects of contraction of the several chambers, the functions of the valves of the heart, the phenomena accompanying systole and diastole, the systolic output,

the maintenance of a continuous flow, the significance of the pulse in the arteries and veins, and the variations in blood supply corresponding to the varying needs of the different organs of the body. Not only should the student have a good grasp of the conditions of the general circulation and of the pulmonary circulation in adult life, but he should familiarize himself with the conditions existing during fetal life, since they throw light upon some of the pathological states met with in adults.

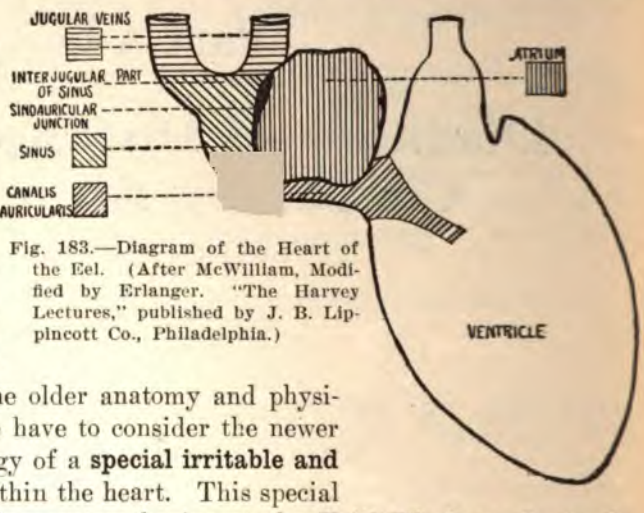

Fig. 183.—Diagram of the Heart of the Eel. (After McWilliam, Modified by Erlanger. "The Harvey Lectures," published by J. B. Lippincott Co., Philadelphia.)

During the last ten years a flood of new light has been thrown upon cardiac pathology through important discoveries that have been made regarding the origin and conduction of stimuli within the heart. To-day, therefore, in addition to the older anatomy and physiology of the heart, we have to consider the newer anatomy and physiology of a **special irritable and conducting system** within the heart. This special irritable and conducting system begins at the **Keith-Flack node** in the sinus venosus at the junction of the superior cava with the right atrium; it includes (1) the walls of the atria, (2) the **atrioventricular bundle of His** (with its intercalated Aschoff - Tawara node) dividing into two limbs: one going to the right ventricle, the other to the left ventricle, and (3) a vast complex of peculiar fibers known as the **Purkinje system** in which the tw... the His bu... nate, and t... stimuli ca... almost si... a whole ... in the

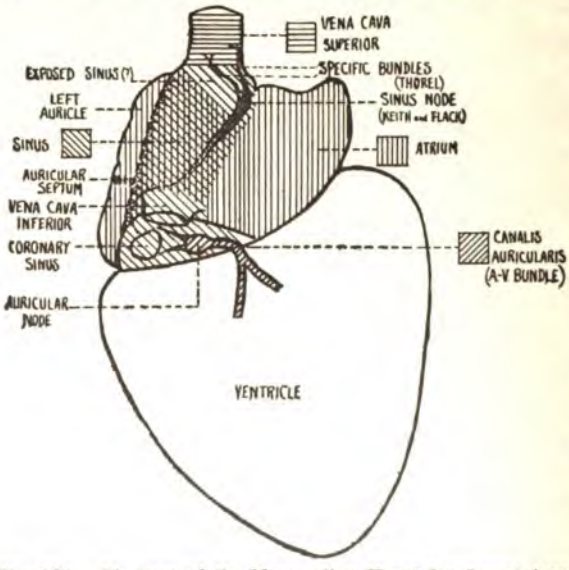

Fig. 184.—Diagram of the Mammalian Heart for Comparison with the Heart of the Eel; the Probable Homologies of the Hearts of Cold-blooded and Warm-blooded Animals are Schematically Represented. (After J. Erlanger. "The Harvey Lectures," published by J. B. Lippincott Co., Philadelphia.)

Under normal conditions, stimuli arise at the Keith-Flack node and are conducted thence to the atria, and, later, through the atrioventricular bundle to the ventricles, so that the different parts of the heart, under normal conditions, contract in regular sequence; the different parts of the organ thus have their activities coördinated in the way best suited to promote the functions that the heart subserves.

Normally, the stimuli originating at the Keith-Flack node furnish the impulses dominant in the irritable system, and though the rest of the system possesses autonomous irritability, this is kept in abeyance. Since all the parts are subordinate, under normal conditions, to the activity of the Keith-Flack node, this node is called the *pacemaker of the heart.* Stimuli to contraction thus normally arising and normally conducted from the Keith-Flack node through the heart are known as **nomotopic stimuli** (from the Greek *nomos*, law, and *topos*, place). Under pathological conditions the normal pacemaker may lose its dominance, and stimuli, arising automatically elsewhere in the irritable system, and known as **heterotopic stimuli** (Greek *heteros*, other, different), may escape control and give rise to abnormal contractions of the heart. Those of us engaged in clinical work owe a great debt to the experimental physiologists (Gaskell, Engelmann, Einthoven, Erlanger, Hirschfelder, Thomas Lewis, Hering, Kahn, Rothberger and Winterberg, Nicolai, Cohn, Frédéricq, and others), who have supplied us with this new knowledge. Its clinical applications will become clear when the cardiac arhythmias are discussed. (See below.)

The automatic activities of the heart are continually being influenced through the inhibitory and the accelerator nerves, or **extrinsic nerves** of the heart. Of these, the *N. vagus* exerts, predominantly, an inhibitory function and the *N. sympathicus*, predominantly, an accelerator function.

The newer studies of **hemodynamics** are also now being applied to a very large extent in clinical work and the experimental studies of the physiologists upon blood pressure, velocity of flow, and the conditions of the vasomotor apparatus generally, have come to have a priceless value for the clinician.

The student who approaches pathological angiology as a clinical career could not do better than to spend a considerable period of apprenticeship in anatomical, physiological, and experimental-pathological laboratories, familiarizing himself with the knowledge concerning the circulation that has already been gained by scientists of these departments, and attempting to make at least some extension of it, before engaging too busily in the clinical work proper.

It is, of course, outside the province of this book to review the anatomy and physiology of the circulation. It must be taken for granted that the student has already acquired a knowledge of the anatomical and physiological facts necessarily precedent to clinical study. In the accompanying [illegible]erences will be found, which, it is hoped, will

guide the reader to the anatomical and physiological sources should he wish to consult them.

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sion of the cardiac dullness; and (3) the delimitation of the margins of the heart by means of Röntgen rays.

(*a*) *The Determination of the Position of the Apex Beat of the Heart*

An elevation of the chest-wall, at regular intervals, at the times of the systoles of the left ventricle can, in the healthy person, usually be seen and felt in the fifth intercostal space of the left side, between the mammillary and the parasternal lines.

As the site of the apex beat we designate the most lateral and the lowest part of the area of pulsation; as a matter of fact, the "apex beat" thus recorded does not actually correspond to the position of the heart's apex, for x-ray examinations show that the latter always lies a little lower. Moreover, the point of maximal impulse (*p. m. i.*) is not always at the site of the apex beat.

In early childhood the apex is in the 4th intercostal space nearer the nipple. The position of the apex beat on standing is practically the same as in the recumbent position. On deep inspiration, however, the apex beat may lie behind the 6th rib or in the 6th intercostal space and be more feebly felt, while on deep expiration it may rise as high as the 4th intercostal space and become more diffuse. The position changes when the patient lies on his left side; it may then reach the mammillary line, or, often, a point two centimeters to the left of it. (After rapid emaciation this mobility may be greater; see "wandering heart.") When the patient lies on his right side, the apex is very little displaced to the right, rarely passing to the right of the left parasternal line.

The position of the apex beat varies somewhat with alterations in the size and shape (long, short, or flattened) of the thorax, a fact that students soon meet with in their clinical experience. Anything that lowers the diaphragm also lowers the apex beat; anything that raises the level of the diaphragm (meteorism, ascites, pregnancy, abdominal tumors) will raise the position of the apex beat. Fluid or air in one pleural cavity will displace the apex beat toward the opposite side; retraction of a lung (fibroid phthisis) will have an opposite effect. Enlargement of the left ventricle alone displaces the apex downward and to the left; enlargement of the right ventricle alone displaces the apex to the left but not downward. A pericardial effusion may displace the apex beat upward to the 3d intercostal space.

Too much stress should not be laid upon slight abnormal position of the apex beat. Its determination, however, is the n the attempt to ascertain the position and size of the heart, in· the position of the apex indicates the situation of the left ma heart.

Precordial Boss or Voussure.—This is the name given to

bulging occupying the precordial area, due to enlargement of the heart or to pericardial effusion. The enlargement is oval in form, its long diameter being vertical and extending from the third to the sixth rib near the sternum. It can arise only in early life when the ribs are still flexible. It should not be confused with the deformations, usually bilateral, due to rickets or to emphysema.

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(*b*) *Determination of the Areas of Cardiac Dullness by Percussion*

We are able by percussion to outline upon the anterior surface of the chest two areas, (1) that of the *superficial, small* or *absolute cardiac dullness*, and (2) that of the *deep, larger* or *relative cardiac dullness*. The area of absolute dullness corresponds anatomically to the part of the sternocostal surface of the heart not covered by the lungs, while the area of relative dullness corresponds anatomically to the whole heart in orthogonal projection. The area of superficial dullness is outlined by very feeble percussion along the margins of the right and left lungs where they overlap the heart. Inside the boundary of this area the characteristic resonant pulmonary note is entirely absent. The larger area of relative dullness is outlined by percussing from the lungs toward the heart and marking the points at which the percussion note becomes less resonant or relatively dull. Though the heart is covered by the lungs at its periphery, the change in the percussion sound elicited permits one to outline its margins with reasonable accuracy. The determination of the superficial dullness is a much easier procedure than that of determining the deep dullness; for the latter a degree of skill, obtainable only by considerable practice, is required.

i. The Area of Absolute (or Superficial) Cardiac Dullness

At the level of the sternal end of the fourth costal cartilage on the left side, the margins of the two lungs begin to diverge; the area between them below this level is that of the absolute (or superficial) cardiac dullness. The margin of the left lung passes to the left along the lower margin of the fourth costal cartilage and then forms a slight convex curve lateralward and downward to the apex. The margin of the right lung passes downward behind the sternum and a little to the right toward the sternal end of the fifth and sixth costal cartilages of the right side. In many textbooks the right margin of the superficial cardiac dullness is said to correspond with the left sternal margin, but in many cases by very careful feeble percussion it is possible, despite the plexímeter action of the sternum, to outline the margin of the lung behind the left half of that bone. It is seldom possible, however, exactly to delimit the margin of the lingula of the left lung; it is so very thin that it influences the percussion note but little.

To outline the superficial cardiac dullness one percusses very lightly with the middle finger of the right hand, using either the index finger, or the middle finger, of the left hand as a plexímeter. Some prefer to place the tip of the flexed terminal phalanx of the plexímeter finger vertically upon the surface of the thorax and to percuss proximal to the joint. One may begin the percussion in the dull area and mark the points at which the lung resonance appears, or one may pass in the opposite direction, marking the points at which the lung resonance goes over into the so-called absolute dullness. It is customary to determine first the right margin of the absolute dullness, then the upper margin and finally the left margin. It is to be borne in mind that the percussion sound is not always absolutely flat like the sound over the thigh, for it may present a slightly tympanitic quality owing to the proximity of the stomach.

Anything that influences the position of the edges of the lungs (*e. g.*, respiration, changes in the position of the body, etc.) will also influence the size of the area of absolute cardiac dullness.

The outline of this area tells us very little about increase in the size of the heart as a whole, though it may be of value as a clew to enlargement of one of the chambers of the heart or of the pulmonary artery. If the edges of the lungs are not adherent, if there be no retraction nor distention of the lungs, and further, if the heart itself be not dislocated, c. the area of absolute cardiac dullness may be helpful in diagno enlargement of either ventricle will lead to displacement of th the lungs and will increase the area of absolute dullness. This cially when the right ventricle is enlarged, in which event the r of the area as percussed out sometimes takes the form of a s (Krönig), instead of the straight vertical line obtained in n

tions. An accumulation of fluid within the pericardial cavity also enlarges the area of absolute dullness; the right margin of the area then forms an obtuse angle with the upper margin of absolute liver dullness.

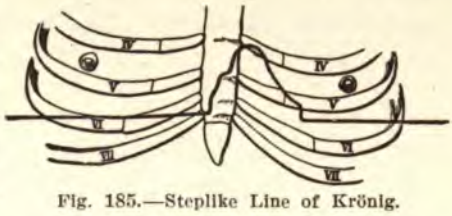

Fig. 185.—Steplike Line of Krönig.

When the area of absolute dullness extends upward along the left margin of the sternum as far as the second intercostal space (*chimney-shaped dullness*) we may suspect the existence of either a dilatation of the left atrium (*e. g.*, in mitral disease), or a dilated pulmonary artery (*e. g.*, along with a patent ductus Botalli).

ii. The Area of Relative (or Deep) Cardiac Dullness

Of far greater value for the formation of a judgment as to the size of the heart as a whole is *the determination of the relative* (or deep) *cardiac dullness.*

To outline it, one does best to use the **method of Moritz,** who percusses with *moderate* force as follows: (1) From the right mammillary line toward the left until a diminution in resonance corresponding to the *right margin* of the heart is reached. The pleximeter finger should be held parallel to the long axis of the body, the patient being told to hold the breath at the end of deep expiration since the right margin of the heart is not dislocated during expiration (though the left is) and the lessened volume of lung over the heart makes the delimitation of the right margin much more easy. Normally this right margin is met with about a finger's breadth to the right of the right sternal margin or about 3.5 to 4.5 cm. to the right of the median line; the percussion note becomes shortened there and of higher pitch. One percusses at different levels and outlines the whole right margin of the heart and higher up the right margin of the area occupied by the great vessels. (2) The lower part of the *left margin* of the heart is best outlined by percussion with less force, the patient making shallow respirations. Here, also, the pleximeter finger is held parallel to the long axis of the body. (3) In percussing out the *upper part of the left margin* of the heart, the pleximeter finger is held transversely to the long axis of the body, beginning at the left margin of the sternum and percussing from above downward, using considerable force. Above the heart, one also determines the presence or absence of dullness to the left of the sternal margin in order to ascertain whether or not the great vessels extend further to the left than normal.

The *upper limit* of the relative cardiac dullness is usually situated between the third and fourth ribs, the *right margin* about a finger's breadth to the right of the right sternal border (3.5 to 4.5 cm. from the median line), though in advanced life it is not uncommon to find no relative dull-

ness to the right of the sternum. The *left margin* of the relative dullness usually corresponds to the position of the apex beat (normally 8 to 9 cm. lateral from the median line), but it may lie still further lateralward if the thorax be narrow or if the heart be relatively large.

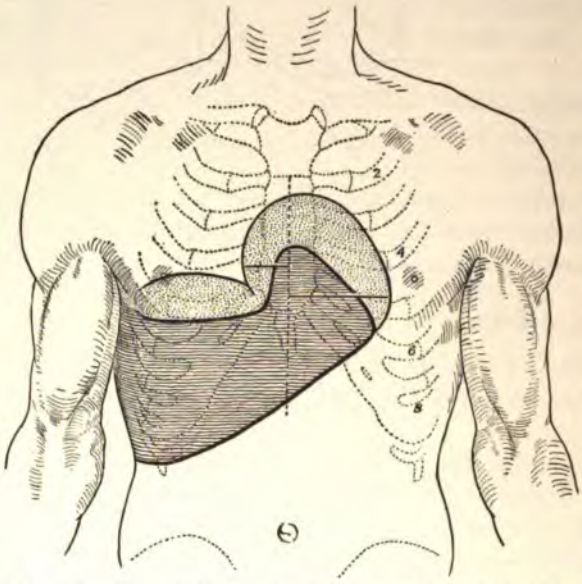

Fig. 186.—Normal Percussion Areas of Liver and Heart. The Dotted Area Denotes Relative Dullness; the Darker Area Absolute Dullness.

One should make it a point to examine patients as far as possible in the same position, inasmuch as posture influences the area of cardiac dullness. In obesity and in emphysema, the determination of the relative dullness is very difficult and the area obtained is often much smaller than that corresponding to the true dimensions of the heart. Much less stress is, therefore, to be laid upon diminution of the area of relative dullness as a sign of a small heart than upon enlargement as a sign of a large heart. When the relative dullness exceeds the normal limits, passing, for example, to the right as far as the right parasternal line or farther, and upward as high as the second rib, while the left margin of the heart is as far or farther to the left than normal, it is certain that the heart is enlarged.

Several other methods of determining the area of relative (or deep) cardiac dullness have been introduced besides the one recommended above. Among them may be mentioned (1) the threshold-value percussion of Ewald-Goldscheider and (2) the palpatory percussion of Ebstein. The student will do best to begin with the method recommended above; later on, if he desire to do so, he may familiarize himself with the special methods mentioned. Above all, the student should avoid the very forcible percussion formerly in vogue. When possible, one should control his technic of percussion by orthodiagraphy or teleröntgenography until [illegible]e results are obtainable.

Enlargement of the Area of Relative Dullness.—This may be either to (1) enlargement of the heart, or (2) pericardial exudate.

When due to *enlargement of the heart* itself, the size depen[illegible] upon dilatation, the changes resulting from hypertrophy alone r[illegible]

sufficient to cause any marked increase of the area of dullness. Dilatation of the left ventricle causes an expansion of the area of relative dullness toward the left only, almost never toward the right. Dilatation of the right ventricle displaces the right margin of the area of relative dullness to the right. When both relative and absolute dullness are increased to the right of the sternal margin, we have to deal usually either with a dilatation of the right atrium or with a pericardial exudate.

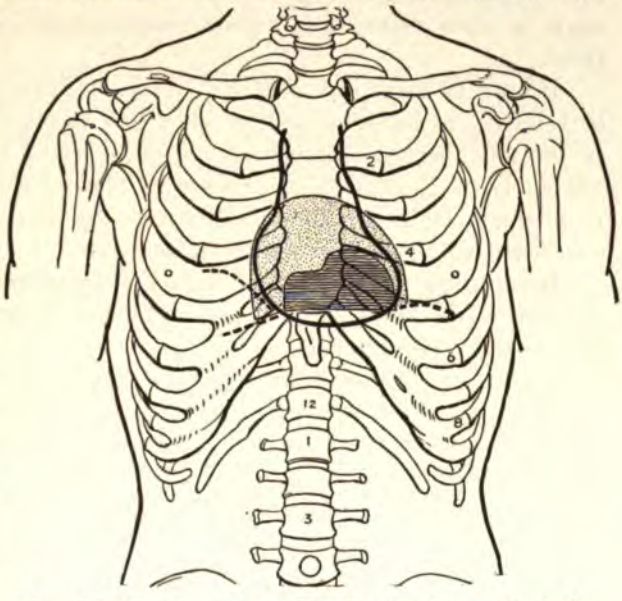

Fig. 187.—Relative and Absolute Cardiac Dullness With Enlarged Right Ventricle and Auricle.

When a *pericardial exudate* is present, the areas of cardiac dullness, both relative and absolute, are increased in all directions; they assume the form of an equilateral triangle, the apex of which is situated above, the right lateral margin extending to the right as far as the parasternal line or farther, and the left lateral margin extending to the left beyond the region of the apex beat. The line of the right margin of dullness may then form a very obtuse angle with the line delimiting the lower margin of the right lung (*i. e.*, with

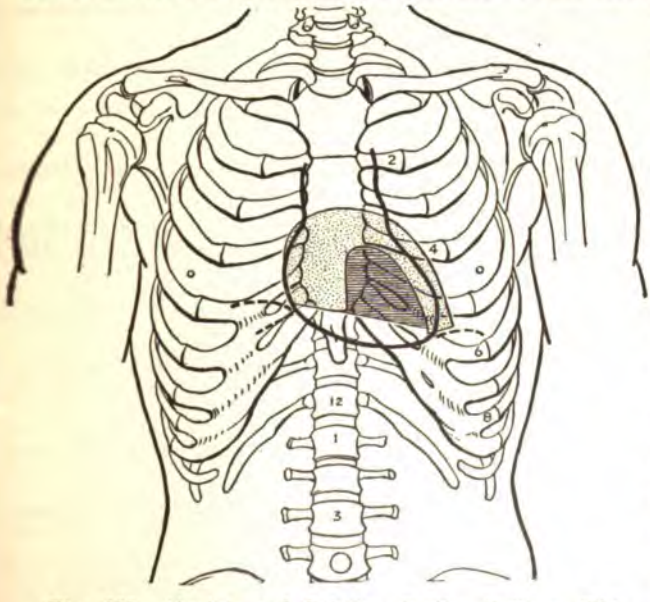

Fig. 188.—Absolute and Relative Cardiac Dullness With Enlarged Left Ventricle.

the line delimiting the upper limit of the absolute hepatic dullness). The angle is often referred to as the "cardiohepatic angle" or the "angle of Rotch."

It must be borne in mind that the area of heart dullness (either absolute or relative) as outlined may be increased through the presence of tumors in the neighborhood, of pleural effusions, or of infiltrations of the lung. Similarly, a dislocation of a heart of normal size by a pleural effusion, by a tumor, or by a pneumothorax may simulate an abnormal position of one heart boundary due to enlargement.

Diminution of the Area of Relative Dullness.—This seldom indicates diminution in the size of the heart; most often the diminution of the area is due to emphysema.

Instead of cardiac dullness one may meet with a tympanitic or metallic sound in cases of *pneumopericardium;* this alters with the position of the patient, in contrast with the persistently resonant, non-tympanitic percussion note that replaces the cardiac dullness in cases of *emphysema of the mediastinum.* In *transposition of the viscera,* the area of cardiac dullness has a topography on the wall of the thorax corresponding to the mirror-picture of that normally met with.

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(c) *Determination of the Size and Position of the Heart by Means of Röntgen Rays*

The most accurate method of determining the size and position of the heart is by means of transillumination of the thorax with Röntgen rays. Either simple fluoroscopic examination (röntgenoscopy) may be employed or actual photographs may be made (röntgenography).

i. Simple Röntgenoscopy

The view of the patient obtained varies according to the direction of transillumination (sagittal, frontal or oblique).

Sagittal View.—When the rays are thrown in from behind at the level of the fifth thoracic spine, and the fluorescent screen is placed in front of the thorax, the transillumination is said to be sagittal and dorsoventral. The heart and great vessels (together with the sternum and the spine) appear as a large median shadow situated between the two pale triangular rib-shaded lung areas, the whole picture being bounded below by the shadows due to the rise and fall of the diaphragm. An examination of the median shadow, known as the CARDIOVASCULAR STRIPE, shows that it is narrower above than below and that it presents characteristic boundary lines. The *right margin* is only slightly curved but nevertheless can be seen to consist of two parts; the upper part above the third rib corresponds to the right margin of the vena cava superior, whereas the lower part below the third rib corresponds to the right atrium. The *left margin* of the shadow presents three curves of which the upper one (I), extending between the first and second ribs, is due to the edge of the aorta; the middle one (II), somewhat flatter, extending between the second and third ribs, corresponds in its upper part to the A. pulmonalis and in its lower part to the left atrium; whereas the lowest of the three curves (III), and much the longest, extending downward and lateralward from the third to the seventh rib, is due to the left margin of the left ventricle.

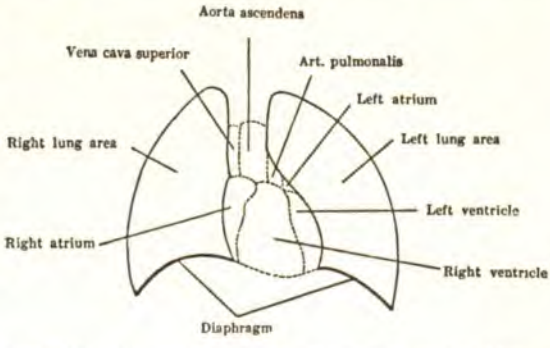

Fig. 189.—Normal Cardiovascular Stripe on Röntgenoscopy. Schematic Representation of the Röntgenoscopic View of the Thorax on Dorsoventral Sagittal Transillumination. (After T. Brugsch and A. Schittenhelm.)

When the thorax is looked through in the opposite direction (ventro-

dorsal sagittal transillumination), the shadow becomes somewhat broader owing to the greater proximity of the heart to the anti-cathode and the consequent enlargement of the projection of the heart on account of the diverging rays.

Frontal View.—On frontal transillumination, the patient holds his arms above his head and the tube is placed in one axillary line while the fluorescent screen is applied to the opposite side; both tube and screen are held parallel to the median plane of the body. A wholly different view is now obtained. Two small lighter areas appear; one of these, lying ventralward, is triangular in shape and is known as the *retrosternal area;* the other lies dorsalward behind the heart and above the diaphragm and is known as the *retrocardial area.* Between these two light areas is the shadow due to the heart. The part of this shadow that forms the posterior inferior boundary of the retrosternal area is due to the right atrium, the conus arteriosus of the right ventricle and the ascending portion of the arch of the aorta. Between the retrocardial area and the spine lie the esophagus and the descending aorta. Unfortunately, frontal transillumination can be satisfactorily employed only in people that are not too large nor too obese. When one gets a good view, important conclusions can be drawn regarding (1) the ventrodorsal diameter of the heart and (2) the [illegible] sence of [illegible] atations [illegible] ing a [illegible] aorta.

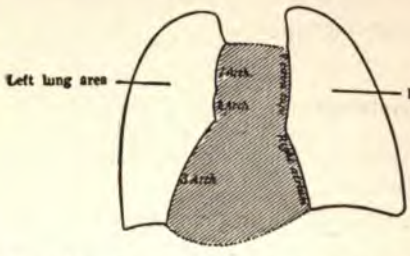

Fig. 190.—Cardiovascular Shadow as Seen on Ventrodorsal Sagittal Transillumination, Schematic. (After T. Brugsch and A. Schittenhelm.)

Fig. 191.—Frontal Transillumination of Thorax, Schematic. (After T. Brugsch and A. Schittenhelm.)

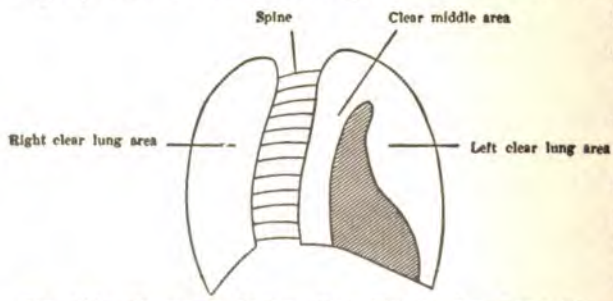

Fig. 192.—Thorax in Oblique Transillumination, Lamp Behind the Left Shoulder, Screen in Front of Right Chest, Schematic. (After T. Brugsch and A. Schittenhelm.)

O
lique

is also useful, though less for determining the size and position of the heart than for examining the condition of the arch of the aorta (*q. v.*).

The simple röntgenoscopic examination is of most value for the study of the movements of the heart (*q. v.*) and for gaining information regarding the general position of the heart and the size of its several chambers. For exact measurements of the heart it is insufficient, and the modification of fluoroscopy known as orthodiagraphy must be employed, or, better still perhaps, Köhler's teleröntgenography (*q. v.*).

Among the **abnormal forms of the cardiovascular stripe** recognizable by röntgenoscopy may be mentioned the following: (1) the so-called "drop heart" (*cœur de goutte* of the French; *Tropfenherz* of the Germans), (2) the senile heart, (3) the type of the enlarged left ventricle, (4) the type of "mitral configuration," (5) the generally dilated heart, (6) the dilated heart in mitral stenosis with tricuspid insufficiency, and (7) the type of pericardial effusion.

In the DROP HEART it is the median position of the stripe, the narrowness of the stripe, the small area in contact with the diaphragm, the

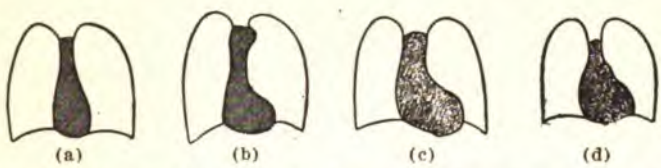

Fig. 193.—Abnormal Forms of Cardiovascular Stripe on Röntgenoscopy. (a) the "Drop-heart" on Dorsoventral Illumination, Schematic; (b) the Senile Heart on Ventrodorsal Illumination, Schematic; (c) Enlargement of Left Ventricle on Dorsoventral Illumination, Schematic; (d) the Mitral Configuration of the Heart of Holzknecht, Dorsoventral Illumination, Schematic. (After T. Brugsch and A. Schittenhelm.)

lateral mobility of the stripe on change of position, the high level of the base of the heart and the exaggeration of the second left lateral curve that are characteristic (Fig. 193 a).

In the SENILE HEART, due to the loss of elasticity and elongation of the aorta, the heart is more transverse than normal (Fig. 193 b).

In the third type mentioned, due to HYPERTROPHY OF THE LEFT VENTRICLE, the heart also lies more transversely. The lowest of the three curves of the left border of the cardiovascular stripe forms a projection that has been compared to a sheep's nose and the heart's apex is plump and rounded (Fig. 193 c).

In the HEART OF "MITRAL CONFIGURATION" (Holzknecht) there is marked exaggeration of the lower curve on the right due to enlargement of the right ventricle and a characteristic bulging in the region of the middle curve on the left due to enlargement of the left atrium and dilatation of the pulmonary artery (Fig. 193 d). When there is aortic insufficiency the second curve on the left may be less marked than normal (Baetjer).

In the UNIFORMLY DILATED HEART the cardiovascular stripe is broader than normal and the widening of the vascular area is especially noticeable owing to dilatation of the vena cava superior (Fig. 194 a).

The heart assumes a peculiar shape in MITRAL STENOSIS ACCOMPANIED

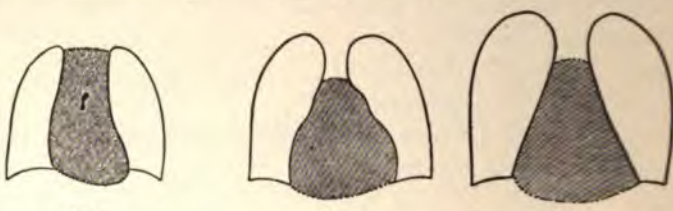

Fig. 194.—Abnormal Forms of the Cardiovascular Stripe (Continued). (a) the Generally Dilated Heart, Dorsoventral Illumination; (b) Dilatation of the Heart in Mitral Stenosis and Relative Tricuspid Insufficiency, Dorsoventral Illumination, Schematic; (c) the Shadow in Pericardial Effusion, Dorsoventral Illumination. (After T. Brugsch and A. Schittenhelm.)

BY TRICUSPID INSUFFICIENCY. Here in addition to the characters of the heart of mitral configuration (*vide supra*) the effects of the great enlargement of the right ventricle and right atrium are visible and the cardiovascular shadow occupies a more median position in the thorax (Fig. 194 b).

When there is a PERICARDIAL EXUDATE, the normal curves delimiting the cardiovascular stripe laterally are obliterated and one sees the straight sides of a dark triangular shadow (Fig. 194 c).

Most important information is given by röntgenoscopy in the diagnosis of DILATATION OF THE AORTA and of AORTIC ANEURISM.

A *diffuse dilatation of the aorta,* so common in people past middle life, especially when arterial hypertension has existed for some time (as in arteriolar nephropathy) or where a chronic luetic aortitis has existed, is easily visible through the fluoroscope.

In *aneurism of the thoracic aorta* there is usually a sharply circumscribed shadow undergoing active pulsation connected with the aortic shadow. The pulsation is expansible in all directions. If an aneurismal sac be partially or completely obliterated by lamellated clots, the pulsation may be slight or absent. For illustration see Aneurism (Special Diagnosis).

To determine which part of the thoracic aorta has undergone aneurismal dilatation, transillumination in oblique directions is desira
is sometimes difficulty in distinguishing an aneurism from tur
larged glands lying upon the aorta and pulsating with it, but
diaphragm be used, the shadow due to aneurism can usually
go over more smoothly into the aortic shadow than does that
a tumor mass. Moreover, the margin of the sac in aneuris
sharply circumscribed and the expansion during pulsatio
all directions.

In *aneurism of the innominate artery,* the shadow lies high to the right and the trachea is usually displaced to the left. The aneurism sometimes appears as a sharp, noselike projection of the arch of the aorta into the left lung area (Külbs).

In *aneurism of the descending aorta,* röntgenoscopy is rarely sufficient for positive differentiation from tumors.

In *aneurism of the pulmonary artery,* the shadow is usually situated in the second right intercostal space and can rarely be differentiated from the shadow of the aorta itself.

In ARTERIOSCLEROSIS, lime deposits in the peripheral arteries can often be demonstrated by röntgenography. In obscure neuralgias of the extremities and in intermittent claudication, röntgenography may be helpful in diagnosis. In sclerosis of the coronary arteries there is rarely calcification enough for recognition in x-ray plates. Calcification of the renal arteries is sometimes demonstrable in the röntgenogram.

ii. Orthodiagraphy

Another method of which much is heard nowadays is the *orthodiagraphic study of the heart.* In it, the attempt is made to determine very accurately the size of the heart by obtaining by successive orthogonal projections a number of single points in the outline yielded by x-rays falling perpendicularly upon the fluorescent screen, all divergent rays being cut off by a diaphragm. The lines joining the points obtained form a figure called the *orthodiagram* (Figs. 196 and 197). Certain distances on these orthodiagrams are measured and the results compared with normal values. The method is valuable for research work; the results exceed in accuracy those of any other method yet invented, except teleröntgenography, but for practical clinical work we can get along very well without orthodiagraphy provided we utilize the other forms of röntgenoscopy to the full, together with accurate methods of percussion. I think it probable that orthodiagraphy will soon be entirely displaced by teleröntgenography.

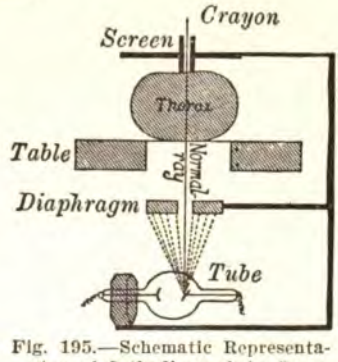

Fig. 195.—Schematic Representation of Orthodiagraph in Cross-section.

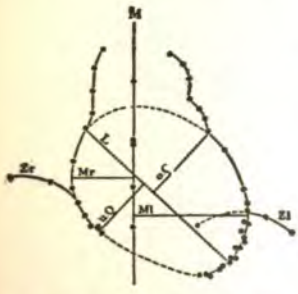

Fig. 196.—Sagittal Orthodiagram. (After Moritz.)

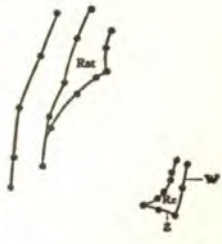

Fig. 197. — Frontal Orthodiagram. (After Moritz.)

The size of the heart, and accordingly of the silhouette of the heart obtained in the orthodiagram, varies within certain limits in healthy people. The heavier the body and the greater the height of the person, as a rule, the larger his heart. In women, the measurements are usually about half a centimeter smaller than in men of the same size and weight. In adolescence, the measurements are somewhat smaller than in adult life; in old people, the measurements are as a rule somewhat increased.

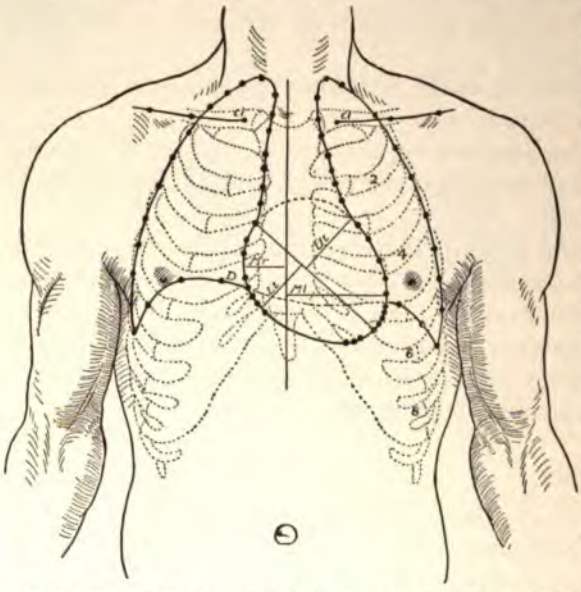

Fig. 198.—Orthodiagram of the Heart, Lung Area, and Diaphragm of a Normal Man. Cl, Clavicle; D, Diaiphragm; Mr, Distance of Right Border of Heart from Median Line; Ml, Distance of the Left Border of Heart from Median Line; Lt and Ut, Lower and Upper Partial Diameter of the Heart Drawn Perpendicular to Cardiac Axis, and Representing the Width of the Heart.

In the following table, Mr. = maximal distance from median line to right margin of heart; Ml. = maximal distance from median line to left margin; Tr. = transversal diameter (or Mr. + Ml.); L. = length of heart shadow; B. = breadth of heart shadow.

TABLE

ORTHODIAGRAPHIC MEASUREMENTS IN HEALTHY MALE ADULTS (AFTER DIETLEN)

Height and Body Weight	Mr. cm.	Ml. cm.	Tr. cm.	L. cm.	B. cm.	Area in Cm.²
Height, 145–154 cm..... Body Weight, 47 kg.....	3.7	8.5	12.2	13.4	9.6	103
Height, 155–164 cm..... Body Weight, 57 kg.....	4.2	8.7	12.9	14.0		
Height, 165–174 cm..... Body Weight, 64 kg.....	4.3	8.8	13.1	14.2		
Height, 175–187 cm..... Body Weight, 71 kg.....	4.5	9.3	13.8	14.9		

According to Groedel, the following table represents the average values for patients in the upright position:

	Mr.	Ml.	Tr.	L.
Adult man	4.6	8.4	13.0	14.0
Adolescent males	4.1	7.8	11.9	12.7
Adult woman	3.9	8.0	11.9	12.9
Adolescent females	3.7	7.2	10.9	12.1

When the thorax is elastic and of normal shape and the heart of normal size, careful percussion of the area of relative cardiac dullness will be found to agree very accurately with the orthodiagraphic findings. Considerable divergence in results, however, is found under certain circumstances, especially when the heart is much enlarged to the left so as to be close to the lateral wall of the thorax or when the thorax is very narrow. This discrepancy is due to the fact that in orthodiagraphy the outline of the heart is a sagittal projection on a plane tangential to the anterior wall of the chest, while in percussion we have to follow the rounded surface of the chest and thus obtain a figure for the relative dullness the left margin of which will be situated much farther lateralward upon the lateral wall of the thorax. Obviously, in such circumstances, there can be no agreement between the orthodiagraphic projection and the percussion projection of the heart limits, and in such cases the apex beat will lie to the left of the lateral margin of the orthodiagram.

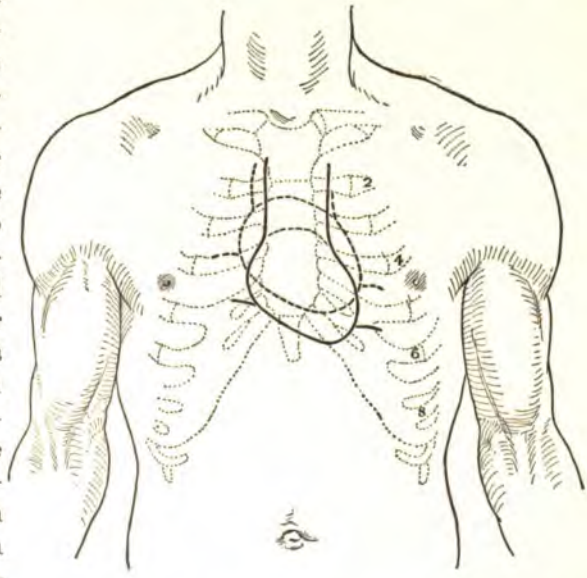

Fig. 199.—Orthodiagram of a Normal Heart. Dotted Line, in Recumbent Posture; Black Line, in Upright Posture. (After Moritz.)

iii. Teleröntgenography

In my own diagnostic work, I now make use of teleröntgenography in place of orthodiagraphy. The method has been described in Part II. It is accurate, expeditious, free from danger and not expensive. I advise its use for the making of permanent records of the exact size and position of the heart.

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C. Cardiovascular Acoustics; Normal and Abnormal Sounds Over the Heart and Vessels

In health and in disease certain oscillations arise in the heart and blood vessels that may cause audible sounds. These can be recognized by listening (*auscultation*) with the naked ear or with the aid of the stethoscope, or the oscillations that are the physical basis of the sounds may be recorded mechanically (*graphic registration*).

1. The Heart Sounds

(*a*) *Normal Heart Sounds*

If the ear be placed over the chest in the cardiac region of a healthy person, *pairs of sounds* are heard recurring at regular intervals. Each pair of sounds consists of a *first* and a *second sound,* separated from one another by a brief interval (the *short pause*). Each pair of sounds in turn is separated from the next pair by a longer interval (the *long pause*). On listening with the stethoscope the duration and accentuation of the single sounds at the apex of the heart is found to be somewhat different from that at the base; thus at the base and over the lower part of the sternum the first sound is longer and more accentuated (rhythm of a trochee ´˘, phonetically indicated as *lúbb-dup* or *tá ta*), whereas at the base the second sound is more accentuated, the rhythm becoming that of an iambus ˘´ (*lubb-dúp* or *ta tá*). The first sound of each pair occurs during the first third of ventricular systole and is therefore synchronous with the apex beat of the heart. The second sound occurs at the very beginning of ventricular diastole. The short pause between the two sounds of each pair is meso- and telesystolic in time, but the long pause separating consecutive pairs is diastolic in time.

(*b*) *Origin of the Normal Heart Sounds*

The origin of the **first sound** of the heart is still in dispute. Physiologists believe it to be chiefly an intracardial-tension-tone due to oscillations set up by vibrations of the walls of the ventricles (muscular, membranous and valvular); the tension of the mitral and tricuspid valves is included here. It is believed by some that the opening of the semilunar valves of the aorta and pulmonary artery and the sudden tension of the walls of the aorta and pulmonary artery also contribute to the sound. The *intracardial-tension-tone* is probably much more important than the so-called *arterial-expulsion-tone.*

Many have attempted to distinguish in the intracardial-tension-tone in turn three sets of components: (1) the tension of the mitral and tricuspid valves; (2) the tension of the semilunar valves of the aorta and pulmonary artery; and (3) the tension of the muscular walls of the left and right ventricles. It seems desirable, certainly, to keep in mind the fact that the normal first sound is due to a combination of the sounds produced in the two ventricles, inasmuch as in disease the components due to either one of the ventricles may undergo alteration. To a certain extent the sounds are analyzable as regards their components by means of auscultation at different areas on the chest wall (*vide infra*). Clinicians are inclined, perhaps, to lay too much stress upon the portion of the first sound due to valve tension to the neglect of that part of it due to tension of the rest of the ventricular wall.

The **second sound** is coincident with and due to the closure and tension of the semilunar valves of the aorta and pulmonary artery at the beginning of diastole; there is general agreement as to the origin of this sound.

In children and young adults a **third sound** is in the majority of cases audible and normal just after what has been described as the second sound. Since it occurs very early in diastole it is designated a protodiastolic sound. It is suggested that it may be due to the floating up of the atrioventricular valves by the blood that rushes into the ventricles before the end of the first third of diastole (Hirschfelder). It is best heard at or near the apex when the patient is somewhat turned to the left side (Thayer). It corresponds to the *h*-wave on the phlebogram.

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(c) *Auscultation Sites*

Since the information yielded by auscultation is of greatest value in determining the state of the various valves and orifices of the heart, the sites that have been selected for auscultation are those at which clinical study, controlled by postmortem examinations, shows the sounds due to the vibration of particular valves to be best heard. These *auscultation sites* for the several valves do not correspond as a rule to the surface overlying the anatomical sites of the valves. The anatomical projections of the valves are situated very close together on the chest wall (Fig. 200); the

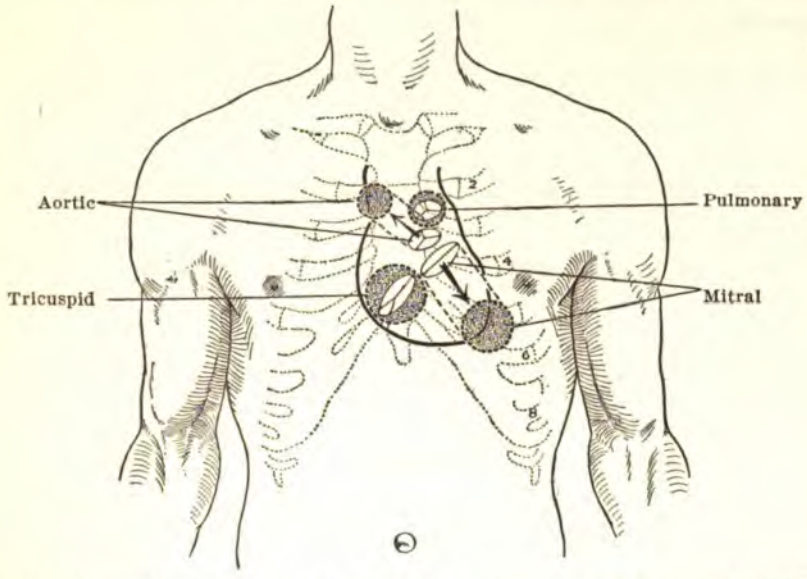

Fig. 200.—Diagram Showing Positions of the Valves of the Heart and the Auscultation Sites.

sites selected for auscultation are relatively widely removed from one another.

Four principal auscultation sites are usually selected:

1. At the apex of the heart, where the muscle tone of the first sound propagated through the whole left ventricle can be heard **(mitral area)**.

2. In the second left intercostal space close to the sternum where the sounds produced by the pulmonary semilunar valves can be best heard **(pulmonary area)**. Here the auscultation site corresponds to the anatomical projection site.

3. In the second right intercostal space close to the sternum **(aortic area)**. Hither the sounds produced at the aortic orifice are well propagated and they can, here, be heard tolerably free from admixture with other sounds.

4. At the junction of the 5th rib with the sternum on both the right and left sides **(tricuspid area).**

It will be noticed that only two of these sites correspond to anatomical projections; namely, the pulmonary and tricuspid. The auscultation site for the aortic valves is not far removed from the anatomical projection site, but the anatomical projection site of the mitral valve is entirely unsuitable as an auscultation site for that valve since the whole right ventricle intervenes between the mitral valve and the anterior chest wall.

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(*d*) *Rhythm and Accentuation of the Heart Sounds*

At each auscultation site, both sounds of the heart are audible, and one must distinguish, at each site, the sound of autochthonous origin from the propagated sound; the former is, under normal conditions, better heard than the latter. Thus, over the pulmonary and aortic sites, the second sounds are autochthonous and the first sounds are propagated, which explains the iambic rhythm (⏑ –) heard there, while at the apex, and in the tricuspid area, the first sounds are louder (autochthonous)[1] and the second feebler (propagated); hence the rhythm of a trochee (– ⏑).

(*e*) *Identification of the Heart Sounds*

There should be no trouble, over healthy hearts, in distinguishing the first sound from the second sound; first, by the accentuation, and, second,

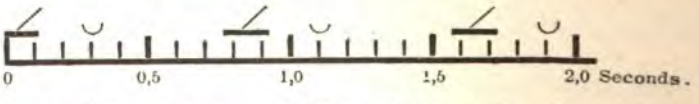

Fig. 201.—Length of Pauses Between the Heart Sounds, in Seconds. (After P. Krause, "Lehrb. d. klin. Untersuchungsmethoden," published by G. Fischer, Jena.)

by the length of the pause following each sound. In disease, t beats may become very irregular (*arhythmia*) or the rate greatly ated (*tachycardia*). In some instances, both the long pause and sound become relatively shortened and the heart sounds then rese ticking of a watch (*pendulum rhythm*) so that the ear may not

[1] At the apex both the first and second sounds are "propagated," but of the first sound is nearer than that of the second.

distinguish which is the first or which the second sound. When this pendulum rhythm occurs with a very rapid pulse, the heart sounds resemble those heard in the fetus (*embryocardia*). If it be impossible by the accentuation of the sounds, or by their relation to the pauses, to tell which is the first and which the second sound, the examiner may help himself out by palpating (simultaneously with auscultation) the apex beat or the carotid pulse. The first sound is synchronous with the apical impulse and precedes the carotid beat by about one-tenth of a second, thus occurring always in the first half of systole. Beginners often make the mistake of trying to time the sounds in all cases by palpation of apex or carotid; clinical teachers should correct this tendency and encourage students to make their decisions by paying attention rather to the accentuation of the sounds and their relation to the pauses, resorting to palpation only in instances where satisfactory timing is impossible otherwise.

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(*f*) *Graphic Registration of the Heart Sounds*

Physiologists and clinicians have devised several methods of registering graphically the time and intensity of the heart sounds, but only two of the more important methods will be here referred to. For full description, the original sources should be consulted.

Einthoven and Geluk's Method.—The Dutch physiologists used a stethoscope attached to a microphone, the current from which was passed through a capillary electrometer, the movements of which were photographed. Later, a strong galvanometer (*q. v.*) was used. Bond, and also Bridgman, have found this satisfactory in the heart station at the Johns Hopkins Hospital.

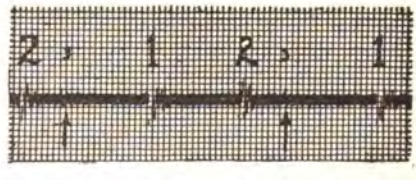

Fig. 202.—The First, Second and Third Heart Sounds as Graphically Recorded by the Method of Einthoven and Geluk. (From A. D. Hirschfelder's "Diseases of the Heart and Aorta," published by J. B. Lippincott Co., Philadelphia.)

Weiss's Method.—Weiss uses a "phonoscope," consisting of a closed chamber containing a small funnel, which is covered by a film of soap bubble. In the center of the film are placed minute capillary tubes, the movements of which are magnified and projected upon a photographic recording apparatus. Gerhartz uses a membrane of collodion instead of the film of soap bubble.

Recently, Crehore's apparatus has been applied by Meara, for the registration of sounds as well as of movements.

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(g) *Detection of Alterations in the Intensity of the Heart Sounds*

The loudness of the sounds of the heart may be less or greater than normal.

i. Enfeeblement of the First Sound

The *first sound* may be enfeebled when something exists that hinders the transmission of the sound (obesity, pulmonary emphysema, large pleural or pericardial effusion). The first sound may also be enfeebled either by defective contraction of the ventricles or by alterations of the atrioventricular valves. A feeble contraction of the ventricle may occur in any of the conditions that give rise to myocardial insufficiency. When vegetations appear upon the borders of the valves the first sound may be diminished or even disappear (*e. g.*, in acute endocarditis).

ii. Accentuation of the First Sound

On the other hand, the first sound may be exaggerated in in
causes operating in the direction opposite to those just menti
the transmission of the sound may be facilitated in emacia
or when there are gas-containing cavities near the heart (
cardium, dilated stomach); in the latter instance the quality
sound may be more metallic than normal. Again, abrupt ven

traction (*e. g.,* in emotional excitement or on physical exercise) augments the first sound, and certain alterations in the atrioventricular valves, such as thickening or induration, may have the same effect. This explains the loud first sound sometimes heard in chronic endocarditis (*e. g.,* mitral insufficiency) and in arteriosclerosis of a mitral cusp.

The accentuation of the individual heart sounds is often of great practical diagnostic significance.

Thus marked accentuation of the first sound at the apex is often a sign of the existence of mitral stenosis. The abrupt first sound heard at the apex in this disease is believed to be due to the more powerful vibrations set up by the sudden tension of the stiffened valve-cusps.

The lesion of mitral insufficiency tends to enfeeble the first sound while that of mitral stenosis tends to exaggerate it. When in the course of a mitral insufficiency the first sound becomes louder and more abrupt, one may infer that stenosis has been added to the insufficiency, and when in the course of a mitral stenosis a mitral insufficiency develops, the first sound may become somewhat feebler.

iii. Enfeeblement of the Second Sound

The *second sounds* of the heart may also be either enfeebled or exaggerated. Though the pressure is much higher in the aorta than in the pulmonary artery, the conditions of auscultation are such that the second sounds, in normal adults, are approximately equal in intensity at the aortic and pulmonary sites. In children, the pulmonic second may be normally louder than the aortic second.

The second sounds may be feebler than normal owing to *faulty transmission* to the stethoscope (in obesity, pulmonary emphysema, pericardial effusion), though in such cases the second sound is usually less enfeebled than the first and if only one sound be audible it is usually the second. Aside from faulty transmission of the sounds, they may be feebler either from *alterations in the arterial valves* themselves (*e. g.,* endocarditis) or from *lowering of tension* in the aorta or pulmonary artery (*e. g.,* myocardial insufficiency, anemia, Addison's disease, tuberculosis, etc.).

iv. Accentuation of the Second Sound

The second sounds may be exaggerated (accentuated) whenever the arterial tension is increased. Thus marked accentuation of the aortic second sound usually indicates hypertension in the aorta; it is frequently met with in chronic nephritis and in some forms of arteriosclerosis.

When in addition to mere accentuation of the aortic second sound there is alteration of the quality or *timbre* of the sound we may usually assume the existence of sclerotic or other changes in the semilunar valves themselves, in which case the second sound besides being loud has a certain

tympanitic or ringing quality. Not only is the character of the sound altered but it seems to be prolonged by a sort of echo or resonance which follows it. In such cases one must take especial care to ascertain whether or not the sound is followed by a diastolic murmur.

Some care must be taken in deciding whether it is the pulmonary second or the aortic second sound that is accentuated in a given case. When the accentuation is maximal to the right of the sternum it is certainly aortic in origin, but when it is maximal to the left of the sternum it is usually pulmonary though it is sometimes due to a sound propagated from the aortic orifice, and other physical signs must be considered in making a decision.

When the pulmonary second sound is accentuated it is evidence of increased pressure in the pulmonary artery and may be due to some obstruction to the flow of blood in the lung (*e. g.*, emphysema, fibroid phthisis, pulmonary arteriosclerosis) or to faulty circulation in the left heart (*e. g.*, mitral disease).

When a pulmonary second sound that has been accentuated becomes enfeebled, it is often an indication of beginning insufficiency of the muscular wall of the right ventricle and is not infrequently coincident with the advent of an insufficiency at the tricuspid orifice.

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(*h*) *Detection of Changes in the Number of the Heart Sounds*

Instead of the first and second sounds of the heart above described, there may be heard, either in healthy or in diseased hearts, three or four or even more sounds (aside from the murmurs which are described later). The additional sounds may be due (1) to failure of the components of the first or second sounds to fuse to a single sound, especially when there is a disturbance in the synchronism of events in the two ventricles, or (2) to the formation of entirely new sounds.

i. Splittings and Doublings of the Heart Sounds (¾ Rhyth

The first sound or the second sound may be *split, double duplicated,* without any marked alteration in accentuation or to the short and long pauses of the cardiac cycle. When the is simply *split,* the fault in coincidence is slight (*tra ta*);

doubled, the fault in coincidence is greater (*ta-ta ta*). Similarly the second sound may be either *split* (*ta tra*), or *doubled* (*ta ta-ta*). Every degree of transition from slight splitting to distinct doubling may be met with. The origin of such splittings and doublings has been much discussed (Geigel, Sahli). These phenomena are frequently met with in health at different phases of respiration; thus the first sound is often split at the end of inspiration and the beginning of expiration, the second sound (less often) at the end of expiration and the beginning of inspiration. The doublings are more common in diseased conditions, and are then audible in all respiratory phases. When the mitral valve is damaged, the second sound is often split or reduplicated at the base, owing to increased pressure in the pulmonary artery. The splitting of the second sound at the apex (*bruit de rappel* of Bouillaud), so common in mitral stenosis, is attributed by some to vibration of the rigid valve when the blood begins to enter the ventricle from the atrium (*claquement d'ouverture de la mitrale*), this giving rise to a sound just after the normal second sound. Many believe that this "cantering" sound is not a true reduplication of the second sound heard at the apex beat, but is, in reality, a divided diastolic murmur that points to mitral constriction.

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ii. Triple or Gallop Rhythms ($\frac{3}{4}$ Time)

The normal 2/4 rhythm of the heart is fairly well maintained in the splittings and doublings above described. Sometimes the heart sounds, however, appear, not in 2/4 rhythm, but as groups of three sounds, of which the first and second and the second and third are separated by approximately equal intervals, while the last member of each group is separated from the first member of the next succeeding group by a somewhat longer pause. In such cases a 3/4 rhythm arises, which, on account of its resemblance to the sounds made by a galloping horse, has been designated *gallop rhythm.* Sometimes the extra sound precedes the first sound of the heart (*presystolic gallop*), sometimes it follows the second sound (*protodiastolic gallop*). In the presystolic type, the three sounds present the

rhythm of an amphibrachy (⏑ – ⏑), in which the middle one is long, the first and last short; in the protodiastolic type, the rhythm is that of a dactyl (– ⏑ ⏑), the first sound being long, and the second and third short. Gallop rhythms are usually most distinctly audible just medial from the apex of the heart, though the rhythm can usually be heard over the whole cardiac area.

The existence of gallop rhythm can be confirmed by palpation, inasmuch as the extra tone is accompanied by a distinct shock palpable at the apex; indeed the tactile features of the rhythm are often more conspicuous than the acoustic. The waves on the mechanically-registered cardiogram should be compared with the waves appearing upon the simultaneously-registered phlebogram.

The significance of gallop rhythms has been much discussed. A protodiastolic gallop is common in bradycardia, in aortic insufficiency and in mitral stenosis. It may be a normal phenomenon when a good normal "third sound" is audible (Thayer). The presystolic gallop is most frequently met with when a hypertrophied left ventricle is beginning to yield to the strain (chronic nephropathy, coronary sclerosis, myocarditis).

Whether the so-called presystolic gallop is in reality presystolic and due to sudden tension of the wall of the left ventricle from vigorous contraction of the atrium (Exchaquet, Johnson) or depends upon a dissociation of the first sound of the heart, the shock due to contraction of the ventricular walls being separated from that due to valve closure (Bard) is still in dispute, though a majority lean to the former view. A slight blowing murmur between the first two sounds of this gallop may be met with when the heart is weak (Lamacq).

The existence of a presystolic gallop rhythm is often more important than that of a heart murmur for diagnosis and prognosis.

While the presystolic type of gallop rhythm most frequently met with seems to be a phenomenon pertaining to the left ventricle, a certain number of cases have been described in which a right-ventricle gallop existed (pulmonary sclerosis). Here the rhythm is best heard in the region of the xiphoid. It has been suggested (on the ground of electrocardiograms) that gallop rhythm is a manifestation of injury to a branch of the His bundle going to one or the other ventricle (Rothberger and Winterberg).

Diastolic Sound in Mediastinopericarditis.—In adherent pericardium there sometimes arises a third sound just after the second sour[illegible] reich thought this due to sudden diastolic expansion of the indrawn thorax (*diastolische Schleuderton*); the sound is hear[illegible] after Brauer's operation of cardiolysis has been performed, explanation is inadequate. Since the sound is accompanied wave on the cardiogram, it is probably due to the inrush of the atrium into the ventricle in diastole and is the ordinary

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2. Heart Murmurs

(a) *Introduction*

From the standpoint of physics, the normal heart sounds, as well as the abnormal sounds known as heart murmurs, are *noises* and never pure tones; they are all due to "aperiodic" vibrations. Some writers speak of the heart sounds as "heart tones" and of the heart murmurs as "heart noises," though as a matter of fact the vibrations of murmurs more often approach the periodicity of clangs or tones than do the normal heart sounds.

The chief difference between the sounds in the normal heart and the heart murmurs met with in disease lies in the duration, and in the termination, of the noise. The normal sounds are briefer, and they die out more quickly. Murmurs tend to be longer, and to fade away gradually. These differences correspond to the origin of the sounds. The normal sounds arise from a single sudden disturbance of the equilibrium of the sound-producing body, while heart murmurs are due to a repeated disturbance of this body; in the normal sounds the duration depends upon the after-vibration of the sounding body dependent upon its inertia, whereas in murmurs the longer duration results from the repeated excitation to movement that occurs (Sahli).

The character of the normal heart sounds is so different from that of heart murmurs that the skilled observer can nearly always recognize the sounds along with the murmurs and uses the former as a frame in which he places the latter.

(*b*) *Analysis of the Features Presented by Heart Murmurs*

In studying heart murmurs, attention is paid to a whole series of features. Of these, some are essential, others less important. Of the essential features may be mentioned:

1. The time (or phase) in the cardiac revolution in which the murmur occurs.
2. The site at which the murmur is best heard; and
3. The direction and propagation of the murmur.

Of the less important features may be mentioned:

4. The intensity of the murmur.
5. Its pitch; and
6. Its quality or timbre.

i. The Timing of Heart Murmurs

The first point to attend to is the exact phase, or the phases, in the cardiac revolution in which the murmur is audible. Clinically, all murmurs occurring between the moment at which the first sound of the heart begins and the end of the short pause marked by the beginning of the second sound are said to be **systolic murmurs**; while all murmurs audible during the period extending from the moment at which the second sound begins to the end of the long pause marked by the beginning of the first sound are said to be **diastolic murmurs.** Obviously, therefore, the perception of the first and second sounds is of greatest importance in determining the time of a murmur.

Systole and diastole (in this clinical sense) may be further subdivided into three portions, a beginning, a middle and an end portion; for the systole these times are known respectively as *protosystolic, mesosystolic* and *telesystolic*, while for the diastole the corresponding terms *protodiastolic, mesodiastolic* and *telediastolic* are employed. Before these terms came into use, murmurs occurring at the end of diastole, just before the systole, were called *presystolic*, and this designation is still in vogue; thus the terms presystolic and telediastolic may be regarded as identic former term, however, is used to describe more particularly those that run into the first sound.

The beginner should avoid the common mistake of think murmur belongs to the phase of cardiac revolution represente sound to which it stands nearest; thus the second sound occupie earliest part of diastole but a presystolic murmur occurring

the first sound of systole is in reality a diastolic murmur, though it is close to the normal systolic sound and far removed from the normal diastolic sound.

When a murmur occupies the whole of systole, it is said to be *holo-*

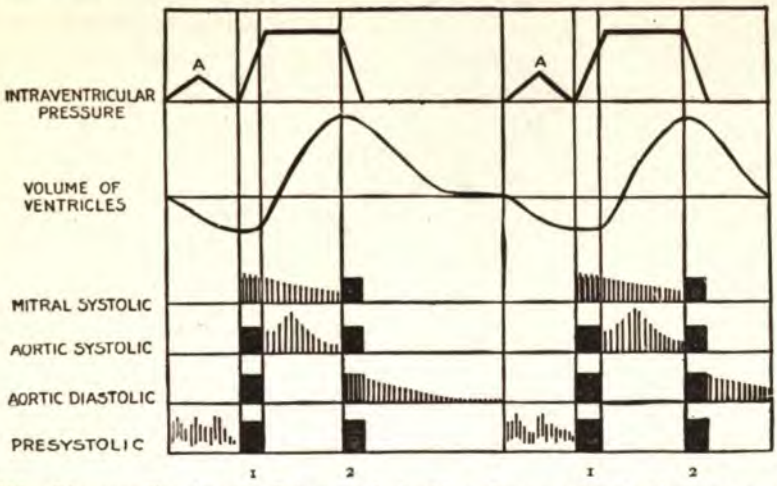

Fig. 203.—Diagram Showing the Relation of the More Common Simple Murmurs to Events of the Cardiac Cycle. Solid Black Bars Indicate the Heart Sounds. Vertical Parallel Lines Reaching to the Base Indicate Blowing or Rough Murmur. Wavy Vertical Lines not Reaching to the Base Indicate a Rumble. (After A. D. Herschfelder, "Diseases of the Heart and Aorta," published by J. B. Lippincott Co., Philadelphia.)

systolic (Gr. *holos,* entire); if it occupies only a part of systole, it is said to be *merosystolic* (Gr. *meros,* portion). Similarly, a murmur may be *holodiastolic* or *merodiastolic.*

When the heart sounds exist in fairly normal relation to the heart pauses, there is but little difficulty in determining the phase of a cardiac cycle to which a heart murmur belongs, even though the accentuation of the sounds deviates from the normal. But in pendulum rhythm, and more especially when one of the heart sounds ceases to be audible, considerable difficulty may be experienced in timing a murmur. One has to be guided in the auscultation then by simultaneous palpation, either of the apex beat or of the carotid pulse.

ii. The Topography of Heart Murmurs

Since the more important cardiac murmurs are due to disease of the valves of the heart, it is desirable to determine whether the location of a murmur does or does not indicate an existing relation between it and one of the orifices guarded by valves. The best auscultation sites for the various valves have been described above in connection with the normal heart sounds. Should a murmur be maximal at one of these sites, it will be designated accordingly; *e. g., mitral systolic* or *mitral diastolic, aortic*

systolic or *aortic diastolic.* One must be cautious, however, as sometimes a murmur *propagated* to one of these areas may be mistaken for one of local or *autochthonous* origin. Thus, a murmur in reality arising at the mitral orifice is often maximal in the pulmonary area and the tyro might

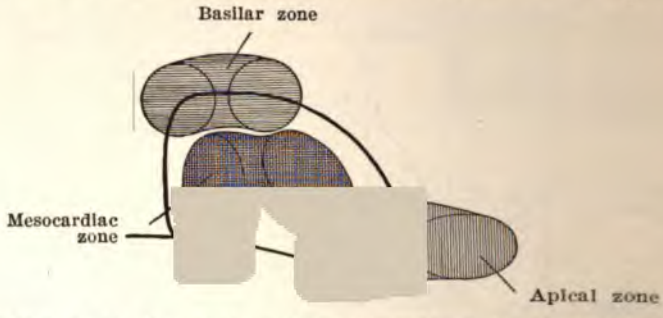

Fig. 204.—Division of the Precordial Area into Zones and Regions. (After Potain; from L. Gallavardin, "Precis des maladies du cœur," published by O. Doin, Paris.)

easily think of a lesion of the pulmonary semilunar valves rather than of the mitral valve.

In describing the exact position of the *puncta maxima,* it is sometimes helpful to use the terminology introduced by Potain (Fig. 204). This author divides the precordial area into three zones:

1. A **basilar zone,** subdivisible into
   (a) A *pre-aortic region,* and
   (b) A *pre-infundibular region.*
2. A **mesocardiac zone,** sudivisible into
   (a) A *sternal region,*
   (b) A *xiphoid region,* and
   (c) A *left preventricular region.*
3. An **apical zone,** subdivisible into
   (a) A *supra-apical region,*
   (b) An *apical region proper,*
   (c) An *endo-apical region,* and
   (d) A *para-apical region.*

Murmurs occurring solely in the left preventricular region and in the para-apical region are usually "accidental" murmurs, not indicating any serious organic disease of the heart. Murmurs audible in the pre-infundibular region sometimes indicate organic disease, thou
often merely functional in nature.

iii. The Direction and Propagation of Heart

Since, as a rule, a murmur is best conducted in the
flow of the current that produces it, it is desirable to a

the point at which a heart murmur is maximal but also the manner in which the murmur is propagated in one or more directions from this point. If, for example, a systolic murmur is produced by narrowing of the aortic valves (*aortic stenosis*), the murmur will be maximal at the auscultation site for that valve in the second intercostal space to the right of the sternum and the murmur will be propagated upward toward the carotid and the subclavian arteries since this is the direction in which the blood flows from the narrowed spot at which the murmur arises.

If the aortic valves leak so that blood can pass back through them into the left ventricle during diastole (*aortic regurgitation*), the diastolic

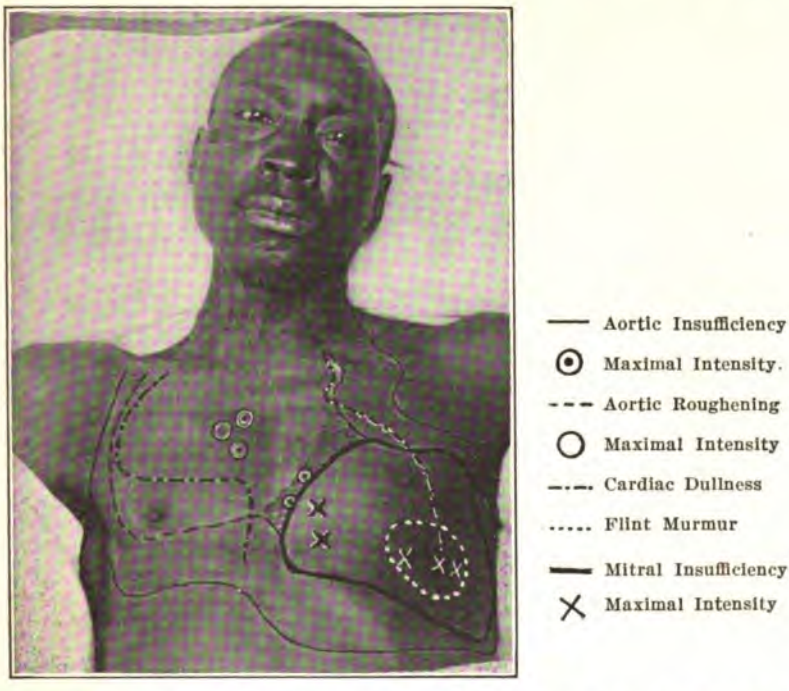

Fig. 205.—Distribution of Heart Murmurs in Man, Age 36, With Aortic Insufficiency, Aortic Roughening, Mitral Insufficiency and Aneurism of the Transverse Arch. (Med. Clinic, J. H. H.)

murmur will be propagated downward and to the left along the left margin of the sternum, corresponding to the direction of the regurgitant flow.

In narrowing of the mitral valve (*mitral stenosis*), the blood is forced through a narrow slit directly toward the apex of the heart and one hears, during the period of the contraction of the atrium, a presystolic murmur in the region of the apex. On the other hand, when the mitral valve leaks and blood regurgitates through it during contraction of the ventricle

(*mitral regurgitation*), the murmur is propagated sometimes best toward the apex of the heart, *i. e.*, in a direction opposite to the regurgitation, by transmission along the chordae tendineae and the papillary muscles (De Sautelle and Grey), sometimes best toward the left atrium, and a systolic murmur may be audible either at the apex, or in the pulmonary area where the auricle of the left atrium comes nearest to the surface.

When *multiple heart murmurs* coexist, a determination of the maximal

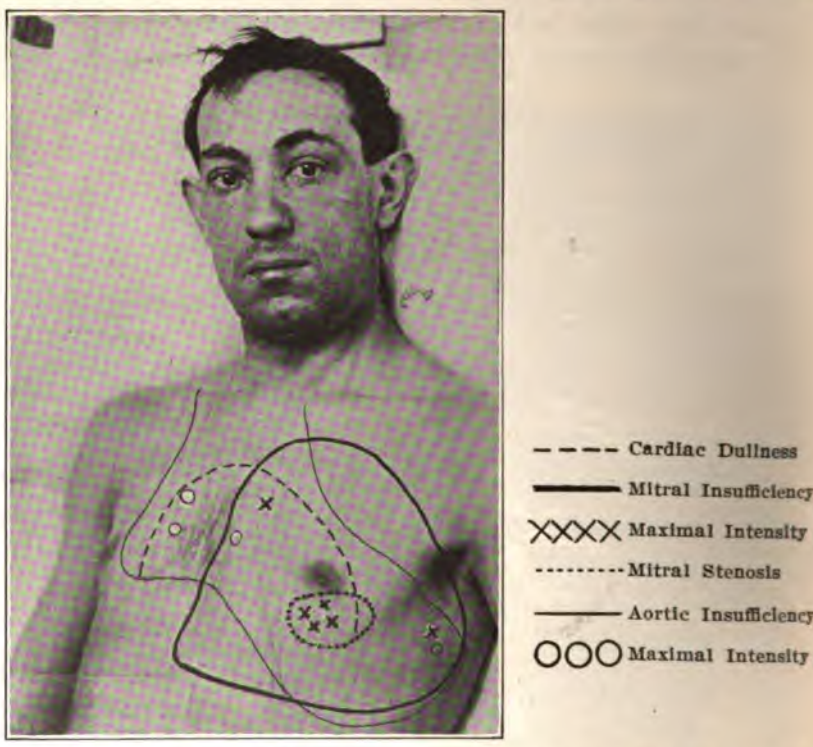

Fig. 206.—Distribution of Heart Murmurs in a Man, Age 33, with Mitral Stenosis, Mitral Insufficiency, and Aortic Insufficiency. Intense Presystolic Murmur at Apex, Ending in Snapping First Sound (Mitral Stenosis); Systolic Murmur at Apex, Widely Distributed Over Chest, Maximal in Pulmonic Area (Mitral Insufficiency); Diastolic Murmur Widely Distributed Over Chest and Axilla, Maximal Along the Sternum (Aortic Insufficiency). (Med. Clinic, J. H. H.)

and minimal points for each murmur and of the direction in which it is propagated is essential for exact diagnosis. One may, for example, hear a systolic murmur in the aortic area and also in the mitral area at the apex, in which event one has to decide whether the former murmur arises at the aortic orifice, or is propagated to the aortic area after originating at the mitral orifice. One may easily make either one of two mistakes; he may, in the first place, assume that a murmur is propagated when in reality both valves are diseased, or he may diagnosticate a defect in both

valves, when, in reality, the murmur in one area is propagated from a distant valve.

A difference in the character of the murmur at the two areas may help to decide; thus, if one be very rough and the other smooth, or if one be musical and high-pitched while the other is soft and blowing, it is probable

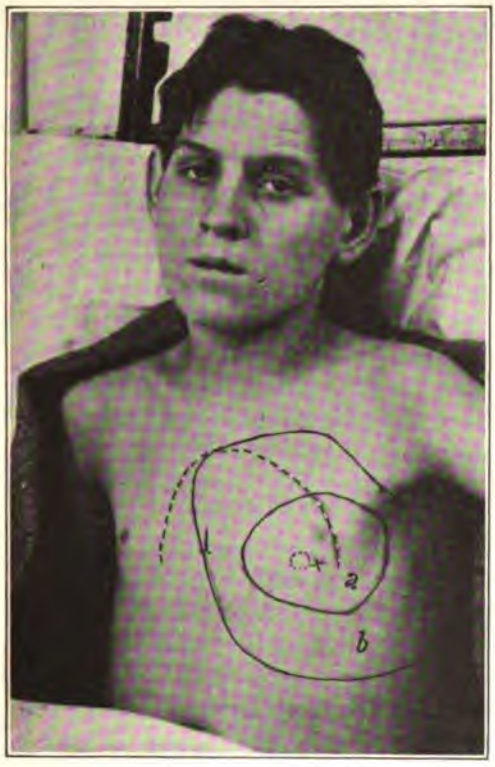

Fig. 207.—Areas in Which Heart Murmurs Were Audible in a Patient Suffering from Acute Rheumatic Fever with Mitral Insufficiency and Mitral Stenosis. Note the Limited Area Just Medial from the Apex of the Heart in Which the Faint Rumbling Presystolic Murmur Leading Up to the Accentuated First Sound Was Heard; Also the Large Area Over Which the Rough Systolic Murmur of Mitral Insufficiency Was Audible, Maximal in an Area of Some Size Around the Apex But Transmitted to the Axilla and the Angle of the Left Scapula. (Med. Clinic, J. H. H.)

that two different murmurs exist, though it has to be borne in mind that a murmur during its propagation may not only be weakened but also, to a certain extent, be modified in character.

In addition to noting differences in the quality of the murmur in the two areas, the intensity should be carefully observed. When the murmur is equally strong in both areas, it is probable that an autochthonous murmur exists at each site, since a murmur propagated any distance is likely to have its intensity lessened. When one murmur is more intense than

the other, the view that the feebler murmur is propagated from the area in which the stronger is heard is favored. If, on listening along a line connecting one area with the other, the sound of the first murmur gradually lessens to a minimum and then increases to a second maximum in the distant area, it is probable that one has to deal with two autochthonous murmurs.

When both systolic and diastolic murmurs are audible over the heart, the diastolic murmur should first be carefully located and analyzed, to the total neglect of the systolic; subsequently the systolic murmurs may be analyzed for themselves.

Occasionally, murmurs are propagated far beyond the precordial region. Thus they may be audible in almost any part of the body—along the spine, in the flanks, in the head as far as the vertex, and even in the limbs. Sometimes a patient may hear his own heart murmur or a person several feet from him may hear it. Such great diffusion was once thought to be characteristic of murmurs occurring in congenital malformation of the heart, but it may accompany any orificial lesion that gives rise to an intense, low-pitched, systolic blow. As a general rule, aortic murmurs are propagated toward the upper part of the body and mitral murmurs toward the lower.

iv. The Intensity of Heart Murmurs

Though the intensity of heart murmurs is very variable, in diagnosis too much stress should not be laid upon this fact. Diastolic murmurs are usually less intense than systolic, though not always. The two factors concerned in intensity are (1) the size of the opening, and (2) the force, or velocity, of the flow. Care should be taken also not to over-estimate the importance of intensity for prognosis. For a very loud murmur may accompany a slight lesion, whereas a very soft murmur may coexist with a serious lesion of the heart. With a given murmur, a patient's condition may be better when it is intense than when it is feeble, since the intensity may, as we have seen, vary with the force of the cardiac contraction.

The intensity of a murmur is in part dependent upon the velocity of flow through the narrow spot at which it is produced; and since the flow is usually quickest at the moment an orifice is opened, most murmurs are more intense at the beginning and gradually fade away; in other words, they manifest a *decrescendo* character. An important exception is the rate of flow through a narrowed atrioventricular valve during ventri- tole. Here the flow is most rapid at the end of diastole, the acceleration depending upon the atrial contraction. This mu therefore approximate to a *crescendo* character.

The flow is probably maximal at the beginning of di normal conditions, but then we have no murmur to point it vanced mitral stenosis, where we have a presystolic murmur,

ditions that cause the murmur also slow the flow and then the greatest flow is probably presystolic in time. Some divide mitral stenosis into three grades:

1. Large opening = murmur protodiastolic.
2. Smaller opening = murmur $\frac{2}{3}$ of way through diastole.
3. Small opening = greatest flow during atrial contraction and murmur is presystolic.

In narrowing of the aortic orifice, the murmur produced may be at first crescendo and later decrescendo.

The intensity of a murmur increases and diminishes with the changes in blood pressure, due to the work done by the heart; thus, when a heart hypertrophies, murmurs in it become intensified, and when a heart weakens, the murmurs may grow feebler.

The intensity of heart murmurs may also be influenced by body posture. Most murmurs are more intense in the recumbent position than on standing; the heart rate is less, and the ventricles contract more energetically. To accentuate the intensity of a heart murmur, one may take advantage of the suggestion of Azoulay, who makes the patient lie down with the head supported, the arms raised and resting gently on the head of the bed, and the lower extremities flexed so that the heels touch the buttocks. In this attitude, the heart is still further slowed and the intensity of a murmur is sometimes markedly increased.

The intensity of a murmur, other things being equal, depends largely upon the size of the orifice at which the murmur is produced. If this be too wide, or too narrow, sound vibrations do not occur; thus, in stenosis of the mitral valve, should the slit become very narrow, the presystolic murmur, or rumble, may entirely disappear; on the other hand, in leakage at the mitral valve, a systolic murmur that has been loud may wholly disappear should the left ventricle, and with it the muscular ring at the mitral orifice, become greatly dilated.

Finally, the condition of the walls of a diseased orifice may affect the intensity of the murmur produced there. Rigid, or calcified, valves may emit loud sounds, whereas soft, fresh thickenings of the valves may give rise only to feeble murmurs.

v. The Pitch, or Tonality, of Heart Murmurs

This depends largely upon the size of the orifice at which the murmur is produced. If it be large, the murmur is likely to be low-pitched; if small, of higher pitch. Very low-pitched murmurs are "rumbling" sounds. In contraction of the mitral orifice, a diastolic murmur may be a rumble of very low pitch, a presystolic blow of much higher pitch, or it may pre-

sent the characters of any one of several gradations between these two extremes.

vi. The Quality, or Timbre, of Heart Murmurs

According to the peculiar quality that heart murmurs manifest, they are designated as blowing, rasping, scratching, filing, musical, aspirative, etc. Though these variations in quality must be due to the physical mechanisms upon which the murmurs depend, these differences are as yet too poorly understood to permit us satisfactorily to value them.

Mitral systolic murmurs are most often blowing in character, aortic diastolic most often aspirative. A musical murmur usually indicates the existence of a vibrating cord in the course of the blood current (loose piece of valve, thickened and retracted chordae tendineae).

(c) *Physical Explanation of the Origin of Heart Murmurs*

Various theories have been advanced but the most generally accepted is that which attributes the origin of heart murmurs to the formation of a "liquid vein," at a point where the blood passes through a narrow channel connecting two cavities. Such a "liquid vein" is prone to be formed at the point where the blood passes through the constriction into the larger cavity. Under normal conditions the relations that exist among the cavities of the heart, the valvular orifices, the velocity of flow and the composition of the blood are such that no murmurs arise, but an abnormal condition of the orifices, a change in the velocity of flow or in the composition of the blood may give rise to a liquid vein, the particles of which vibrate so much that they cause vibration of neighboring parts and give rise to murmurs. Much experimental work has been done in this connection; generally speaking, the greater the velocity of flow, the greater the change in the size of an orifice; the thinner the blood and the rougher the surfaces over which the blood passes, the more easily do murmurs arise and the louder they are. Sometimes, a murmur arises when, through the mechanical conditions existing, one current of blood opposes or conflicts with another.

(d) *Significance of Heart Murmurs*

A murmur audible over the heart may arise inside the heart (*intracardiac murmur*) or outside the heart (*extracardiac or exocar*
A murmur may be produced by organic disease of the heart *murmur*), or it may be independent of such disease (*inorg*
Thus an inorganic murmur may be caused by a relative ins
valves owing to the dilatation of the ring muscle surrou
orifice (*functional heart murmur*) or it may have its orig
not due to disease of the heart muscle or its valves (*accider*

which case it may depend upon an impoverished state of the blood (*anemic murmur*) or upon increased rapidity of flow (*velocity murmurs* in fevers) or upon causes that are as yet unknown to us.

i. Organic Intracardiac Murmurs

Pathological changes in the heart valves due to endocarditis or to atherosclerosis may lead to imperfect closure of the orifice **(valvular insufficiency)**, on the one hand, or to narrowing of the orifice **(valvular stenosis)** on the other. Murmurs due to insufficiency of a valve will be produced in those phases of the heart action during which the orifice is normally closed, whereas murmurs due to stenosis will arise when the orifice is open and the blood current is passing through it in the normal direction. The time relations of the murmurs arising at the four main orifices of the heart are represented in the following table:

TABLE OF ORGANIC MURMURS

Valves	Insufficiency	Stenosis
Aortic and pulmonary	Diastolic	Systolic
Mitral and tricuspid	Systolic	Diastolic

The special characters of these different murmurs will be more fully discussed under the diagnosis of the several diseases of the heart (*vide infra*). As a rule, the murmur in stenosis is rougher and shorter and more likely to be accompanied by a palpable thrill, than the murmur in insufficiency, which is softer and more prolonged. Ingenious methods for imitating the heart sounds and murmurs have been devised by C. W. Larned and by H. L. Smith; they are useful in didactic work.

ii. Inorganic Intracardiac Murmurs

Clinical experience has taught us that murmurs are frequently audible over the heart during life, though at autopsy no changes in the valves of the heart are demonstrable. Such murmurs, independent of anatomical lesions of the valves, have been called inorganic murmurs. That a certain number of these are due to imperfect contraction of the muscle ring around the valve, leading to a **functional** or **relative insufficiency** of the valvular closure, has already been pointed out. Relative insufficiencies of this sort are common at the mitral and tricuspid orifices. They occur occasionally at the aortic orifice (relaxation of Stewart's muscle ring) and

perhaps also, though still more rarely, at the pulmonic orifice (G
Steell murmur "of high pressure in the pulmonary artery").

The term **accidental murmurs** is perhaps better reserved for th
murs that are still less important as regards the condition of th
itself; namely, for those murmurs depending (1) upon slight abn
ties in the course of the contraction of the heart muscle due to ner
other influences, (2) upon abnormal composition of the blood,
upon changes in the velocity of flow.

Accidental systolic murmurs at the apex, or in the pulmonary a
occasionally met with in healthy persons, especially in children b
the ages of 10 and 14.

In all forms of anemia, but especially in chlorosis and in per
anemia, accidental systolic murmurs may be heard over the whole
occasionally an anemic diastolic murmur is audible. Perhaps some
accidental murmurs audible in cachexias may depend upon the
panying anemia.

In conditions in which the action of the heart is excited (fever
rasthenia, Graves's disease), accidental systolic murmurs are often
in the pulmonary area and over the left ventricle. They app
depend in part upon increased velocity of flow and in part upon ir
contraction of the heart muscle.

A certain number of murmurs resembling more or less closely
above described have their origin in the lung during movements
heart (*cardiorespiratory murmurs, q. v.*). I mention them here b
they may closely simulate a murmur of intracardiac origin; th
however, extracardiac in origin. (See below.)

The criteria for differential diagnosis between these less importan
murs and the more important murmurs due to organic disease of the
or to relative insufficiency should be carefully studied. In general,
be said that the less important murmurs are systolic rather than d
and that they are merosystolic rather than holosystolic. They a
precisely localizable than the organic murmurs; some of them occur
in which organic murmurs are often audible (apical and pulmonary
but many of them are heard in areas at which organic murmurs are
present (left preventricular and para-apical regions).

Accidental murmurs are rarely of very high or of very low
they are more commonly soft, aspirative and superficial, though, oc
ally, rough and even rasping, or musical, accidental murm
heard. Further, accidental murmurs are as a rule much n
in intensity than organic murmurs, especially under the int
respiratory movements and of change in posture. Most in
the accidental murmurs are not accompanied by those other
heart and circulation that follow upon organic diseases of
are demonstrable by other physical methods of examinat

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3. Extracardiac (or Exocardial) Murmurs

Among the abnormal sounds audible over the heart, synchronous with its action but arising outside its cavities, are:

(a) Pericardial friction.
(b) Pleuropericardial friction.
(c) Cardiorespiratory murmurs.
(d) Precordial crackling of mediastinal emphysema.
(e) Splashing and water-wheel sounds.

(*a*) *Pericardial Friction Sounds*

The sounds known as **pericardial friction rubs** are due to roughness of the pericardium as a result of fibrinous deposits in acute pericarditis; in rare instances, cancerous nodules in the pericardium may be a cause. They are usually scratching, interrupted and rough; the sounds seem to be superficial, close to the ear. Most often they resemble the sounds emitted when one rubs a piece of silk or a new bank-note between the fingers. Occasionally, the sound is like that of the creaking of a new saddle.

A portion of the sounds occurs during systole and a portion of them during diastole. They are therefore *to and fro sounds,* though the systolic sounds nearly always predominate. Close attention shows, however, that the sounds are rarely strictly related to the beginnings of systole and of diastole; they are more often mesosystolic and mesodiastolic. They may, in rare cases, be limited to the systole, and, still more rarely, to diastole; in the latter case, especially when soft, a pericardial rub may be mistaken for the diastolic murmur of aortic insufficiency. Occasionally, the rub is divided into three parts (*locomotive murmur*), yielding a $\frac{3}{4}$ rhythm resembling gallop rhythm, or the rub may even be divided into four parts, due possibly to successive rubs during systole and diastole of both ventricles and atria.

Pericardial friction is most often heard in the middle zone of the precordial region at the level of the third left intercostal space, but it may be met with at the base in either the aortic or pulmona
occasionally, a rub is audible at the apex. The sounds are
to a rather small area though they are often more
instances, a rub may be widely propagated, even into the b
there be a coexisting pneumonia and the heart be beatin

It should be borne in mind that a pericardial friction
be missed, owing to its feeble intensity, when the heart is

A friction rub is very easily influenced by alterations in the posture of the patient, and by respiratory movements. The intensity is increased with the pressure of the stethoscope. If the presence of a rub be suspected, the patient should be examined in different postures, especially in the sitting position with the trunk bent a little forward; in the right lateral position, it is well to listen especially at the right margin of the heart, and in the left lateral position at the left margin.

As fluid collects in the pericardial cavity and the heart floats on its surface, the rub gradually disappears, remaining longest at the base.

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(*b*) *Pleuropericardial Friction Sounds*

A pulsatile friction sound, produced by rubbing of the outer surface of the pericardium against the pleura, may be synchronous not only with the heart's action but also with the respiratory movements. The portion of the sound due to the latter will cease when the breath is held.

(*c*) *Cardiorespiratory Murmurs*

These sounds, known also as *pulsatile pulmonary sounds* (S. J. Gee), arise in the lungs chiefly during the systoles accompanying inspiration. Occasionally diastolic sounds are produced, and, sometimes, the sounds are audible during expiration also. The heart becomes smaller during systole and the ingress of air in the adjacent lung is increased, owing to greater negative pressure in the lung. The sounds may be blowing like those of vesicular breathing, or crackles and râles may be produced. The systolic vesicular breathing may closely resemble a heart murmur. These pulsatile pulmonary sounds usually cease, or are markedly modified, when the breath is held. They are also much influenced by changes in posture.

When the lung is adherent in front of the vessels at the base of the heart, a diastolic murmur sometimes becomes audible, the diastolic retraction of the aorta causing a localized aspiration into the adjacent pulmonary alveoli.

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(*d*) *Precordial Crackling of Mediastinal Emphysema*

If there be air in the mediastinal tissues (mediastinal emphysema), a crepitant sound, synchronous with the heart's action, may be audible over the heart and may closely resemble the sound emitted by pericardial friction.

(*e*) *Splashing and Water-wheel Sounds*

If air and fluid occur together in the pericardial cavity, each beat of the heart may give rise to a metallic, ringing splash. Similar sounds are sometimes heard when there is a pulmonary cavity near the heart, when a hydropneumothorax exists, or even when the stomach is much distended with fluid and gas. Sometimes the sound resembles the clacking, or chopping, noise made by the floats of a water-wheel (*bruit de moulin* of Bricheteau). The character of this water-wheel sound varies according to the predominance of the liquid or of the gas, or according to their admixture. When the fluid predominates, the sound is crepitating, or resembles a metallic gurgle (Stokes). If the gas be large in amount, the normal sounds of the heart, or any pericardial rubs present, may possess a metallic consonance. The typical water-wheel sound arises when the liquid and air are more or less mixed.

If the water-wheel sound have an extrapericardial origin, it will disappear when the patient is sitting, to reappear when he lies down; but if it be intrapericardial in origin, the sound is heard in both positions (P. Reynier).

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4. Auscultation of the Blood Vessels

When listening over the blood vessels, one must take care not to exert pressure, unintentionally, with the stethoscope; otherwise, a narrowing of the vessel will be produced, which will give rise to a murmur.

(*a*) *Auscultation of the Arteries*

One locates the vessel by palpation and sets the bell of the stethoscope lightly upon it. Normally, two sounds are audible in the subclavian and the carotid arteries, the first just after the beginning of ventricular systole (*arteriodiastolic*), the second just after the beginning of ventricular diastole (*arteriosystolic*). If the artery be pressed upon now with the stethoscope, a ventriculosystolic *stenosis murmur* will become audible; but if the pressure be increased so as to close the vessel, a single tone is heard (*pressure tone*). Occasionally, a single tone (arteriodiastolic) is audible over the abdominal aorta, or over the femoral artery; but no sounds are audible, normally, over the other arteries of the body.

Systolic murmurs due to narrowing at the aortic orifice are often propagated into the carotid and the subclavian arteries. When the aortic second sound is absent, as in some cases of aortic insufficiency, no arteriosystolic tones are heard in the great vessels.

When a Corrigan pulse exists (see Pulsus celer), the pulse wave rising quickly and sinking again very rapidly, an arteriodiastolic murmur is often audible in the arteries of the neck, and an arteriodiastolic tone over the femoral and the brachial and, sometimes, over the smaller arteries. The phenomenon is most often met with in aortic insufficiency, but it may also be encountered in Graves's disease, in fever, and even in nervous palpitation. When a very loud sound is audible, it is spoken of as a "pistol-shot sound."

Arterial murmurs are sometimes audible over the aorta and over the carotid arteries in arteriosclerosis of the aorta; these are supposed to be due to the friction of the blood against the roughened intima.

In aortic insufficiency, on listening over the femoral artery, two tones, quickly following one another, are sometimes to be heard (*Traube's double tone*). On slight pressure with the stethoscope, these tones disappear and one hears, first, a normal pressure murmur, and later, on stronger pressure, a second murmur (*Duroziez's double murmur*). If the pressure be still further increased, one hears only the normal pressure tone. The double murmur of Duroziez may be heard also, sometimes, in chlorosis and in Graves's disease.

Any compression of an artery may give rise to a stenosis murmur. Use is made of this fact in the auscultatory method of determining maximal and minimal blood pressure (*q. v.*).

It is possible that some of the murmurs audible, at times, in the second left intercostal space in pulmonary tuberculosis may be due to compression of the pulmonary artery by the tuberculous changes in the lungs or by enlarged bronchial glands. Similarly, the murmur sometimes audible over the subclavian artery in apical tuberculosis may be due to compression of the artery from pleural adhesions.

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(*b*) *Auscultation of the Right Jugular Vein*

The stethoscope is placed over the sternal attachment of the right M. sternocleidomastoideus, the patient sitting or standing (not lying) with the head turned toward the left.

In the jugular vein certain sounds become audible under abnormal conditions; they include (1) the venous hum, and (2) the venous tone.

Venous Hum.—In anemic patients, especially in chlorosis, and occasionally in healthy people, a continuous blowing, singing or humming murmur, with cardiosystolic accentuation, loudest during inspiration, is audible (*humming-top murmur, bruit de diable*). It is due to the production of a liquid vein in the blood flowing into the widened bulbus of the V. jugularis.

Less continuous, more intermittent, venous murmurs are unimportant.

Venous Tone.—This is sometimes audible, in the same situation, in tricuspid insufficiency; it is due to sudden tension of the dilated vein when the blood propelled by the contracting right ventricle rushes

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D. Methods of Examining the Movements of the Heart and Blood Vessels

The signs of the activity of the heart include the heart sounds (*q. v.*), and certain movements of the heart and blood vessels that are accessible to clinical examination. These movements are visible and palpable as pulsations in the heart and its neighborhood and in the arteries and veins of the body. The movements can be most accurately analyzed by means of instruments of precision yielding graphic records.

1. Inspection of the Movement of the Heart and Blood Vessels

Every examination of the circulatory system should be begun by a careful inspection of the naked parts in which movements of the heart or vessels are visible in normal and abnormal states. The movements include:

1. The *apex beat,* in which inspection is helpful chiefly in the localization of the area of palpation;
2. *Precordial movements,* other than those of the apex beat, including wavelike movements over the right ventricle, retractions at the base and apex, and pulsations in the aortic and pulmonary areas;
3. Movements in the left inferior thorax (*Broadbent's sign*);
4. *Abdominal pulsation;*
5. Visible *pulsations in the peripheral arteries and veins;* and
6. The *capillary pulse.*

The patient should be examined in at least two positions: (a) the *recumbent* position, with the upper part of the body slightly elevated, the patient being kept as quiet and free from emotional disturbance as

possible; and (b) the *sitting* or *standing* position, in profile view, with the eyes of the examiner on a level with the part inspected. On looking for a capillary pulse, the patient's hand should be elevated, and the quick of the finger nails observed for alternating flushing and pallor.

The data of inspection useful in *detecting anomalies of the size* and *position of the heart* have already been referred to under that heading. Here we have to deal with the data useful in the *detection of anomalies in the movements of the circulatory organs.* For convenience, these will be discussed together with the findings that are yielded by palpation and by the application of instrumental methods.

2. Palpation of the Movements of the Heart and of the Blood Vessels

With the hand, most of the movements mentioned under inspection can be distinctly felt, and a number of movements that cannot be seen are recognizable by palpation. Thus, for example, an apex beat that is invisible may sometimes be felt; various invisible shocks and thrills are palpable; and, in addition, details of the movements of the blood vessels that are not accessible to inspection can be made out on palpation.

In practicing palpation, the palm of the hand (the tips of fingers for the pulse) is applied lightly and with varying degrees of pressure upon the area to be examined. One should palpate not only the region of the apex of the heart but also the whole precordial area, the axilla, the vessels in the neck, the epigastric and hepatic regions and the more superficial vessels in various parts of the body, including, of course, the radial pulse.

3. Instruments for Mechanical Registration of Movements of the Circulatory Apparatus

Thanks to the studies of physiologists, clinicians have been able to apply very exact mechanical methods of registration to many of the movements we are here considering. The movements of the walls of the peripheral arteries and veins due to pressure changes within, can be mechanically recorded as sphygmographic pulse-tracings *phlebograms*), and the movements of the apex beat and of tricle in the precordium, by the same or a similar instrume *diosphygmograms.* By registering the pulsations of a colum a stomach tube, as an *esophageal cardiogram,* we have a contractions of the left atrium. Of the many instrumen been devised for these purposes, the two most commonly i

present time are the ink-polygraph of James Mackenzie and the cardio-sphygmograph of Jaquet.

The movements of the heart and aorta can be observed and registered in the form of *röntgenograms* and *cinematograms.*

The electrocardiograph permits us to register graphically the electrical action currents that arise in the heart muscle during the excitation that precedes contraction, and we can, therefore, through the resulting *electrocardiograms,* get information that indirectly informs us of the cardiac movements that immediately follow such excitations.

The volume pulse can be mechanically recorded in the form of *plethysmograms,* and the velocity pulse in the form of *tachograms.*

(*a*) *The Sphygmograph*

Considerable practice is required in order to gain skill in the use of the sphygmograph. The older instruments of Vierordt, Marey, and Dudgeon have given way to the modifications devised by Jaquet and by Mackenzie. The instruments now in use are polygraphic, recording simultaneously the heart tracing (or cardiogram), the arterial pulse tracing (or arteriogram), and the venous pulse tracing (or phlebogram).

i. James Mackenzie's Improved Ink-polygraph

This instrument resulted from the long study of the pulse by James Mackenzie when he was a general practitioner in a small town in England. The apparatus

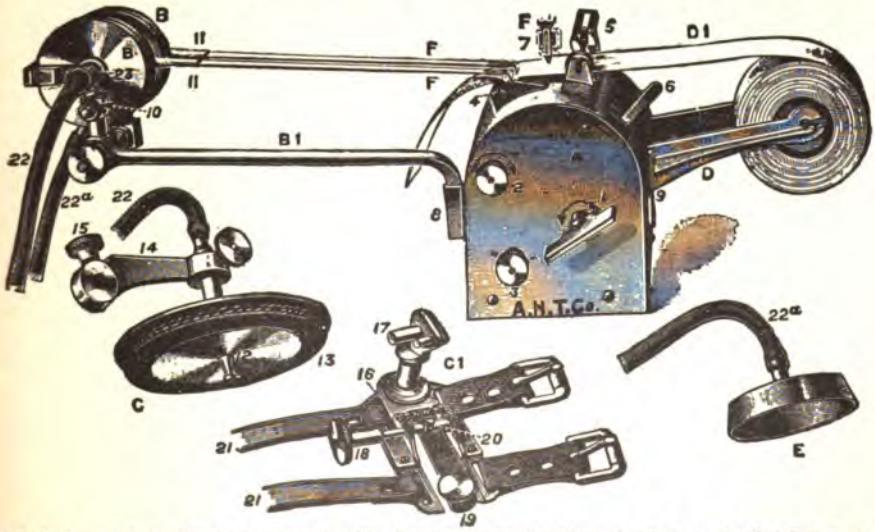

Fig. 208.—This Instrument Records Two Simultaneous Tracings Only, i. e., Radial Pulse, and One Other, Such as Carotid, Jugular, Apex Beat, etc., and Writes With Ink on Glazed Paper. The Clockwork Operates at Variable Speeds. (By courtesy of A. H. Thomas Co., Philadelphia.)

is convenient and is satisfactory for clinical purposes. There are three receivers—one for the heart, one for the vein, and one for the artery. "The levers bear ink pens and write upon an endless roll of white paper."

ii. Jaquet's Cardiosphygmograph

The models now in use make three tracings, simultaneously, in addition to the time-marker curve ($\frac{1}{5}$ sec.).

Fig. 209.—Jaquet Cardiosphygmograph, Two Tambour Type, With Arm Rest, in Position for Recording Brachial Pulse and Showing Cardiograph Attached for Taking Apex Beat and Receiving Tambour for Taking One Other Tracing Such as Jugular or Carotid Pulse. Reproduced from Article by Dr. Geo. W. Norris, "Modern Instruments of Precision in the Study of Cardiovascular Disease," in International Clinics, Vol. IV, Twenty-first Series. (By courtesy of A. H. Thomas Co., Philadelphia.)

iii. Hirschfelder's Modification of the Erlanger Apparatus

This is an ingenious polygraph, "in which two small Marey tambours and a time-marker are arranged to write above the lever of Erlanger's blood-pressure apparatus." When the bag is inflated upon the arm, the brachial pulse is recorded by the lever of the blood-pressure apparatus and this arteriogram is used as the standard instead of a tracing from the radial or the carotid. Curves from the jugular vein and from the precordial area are simultaneously recorded. In Uskoff's sphygmotonograph there is a similar arrangement for recording simultaneously the height of the blood-pressure curve and another tracing from apex, vein, or artery. In Fig. 211, a new portable polygraph that is very satisfactory is pictured.

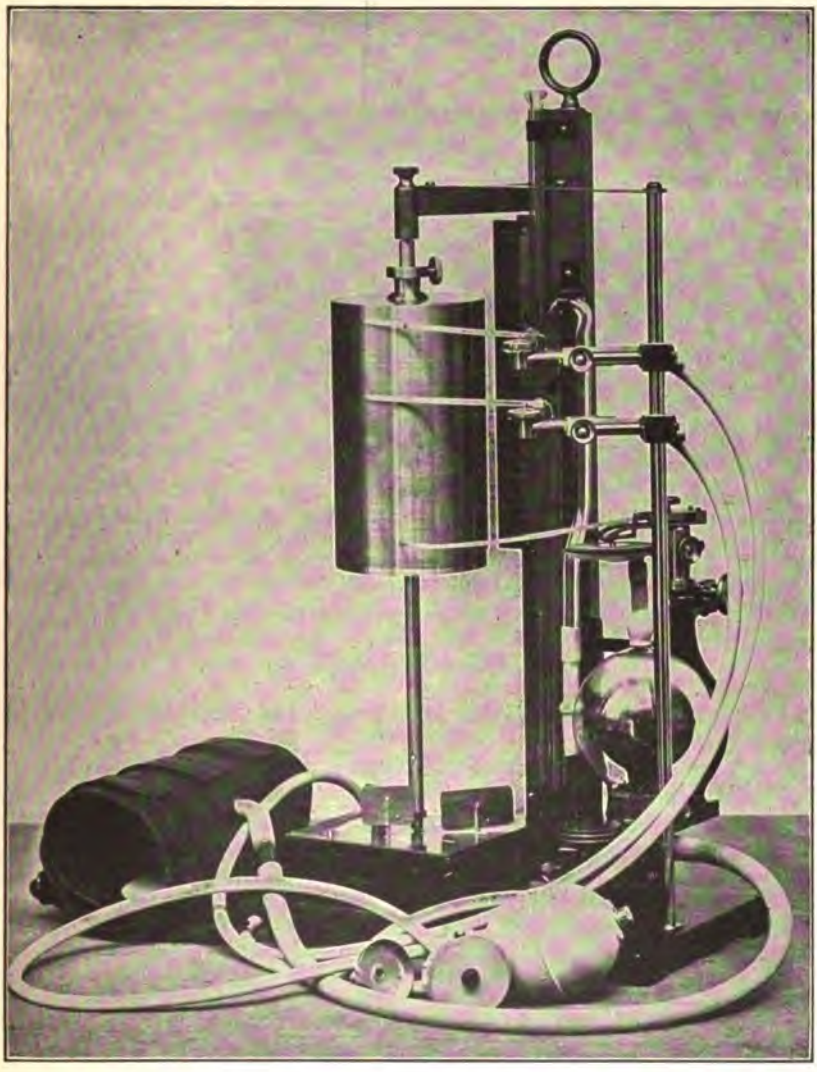

Fig. 210.—Erlanger Apparatus for Determining Maximal and Minimal Pressures, With Hirschfelder's Polygraph Attachment. (By courtesy of Schneider Bros., Jersey City.)

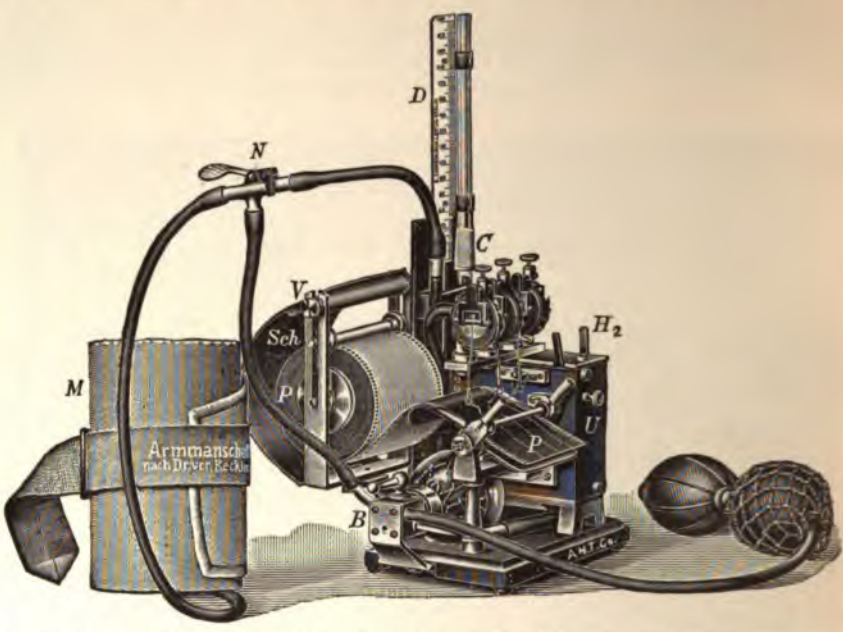

Fig. 211.—New Portable Polygraph. Three Recording Tambours. Sphygmomanometer for Blood Pressure and Cuff for Recording Brachial Pulse Under Varying Pressure. Two Receiving Tambours for Jugular, etc. Cardiograph for Taking Apex Tracing. Rolls of Prepared Smoked Paper 20 Meters Long. (By courtesy of A. H. Thomas Co., Philadelphia.)

iv. Other Sphygmographs

The French instrument of Verdun is an excellent one, as is also A. G. Gibson's upright polygraph.

The micrograph used by Crehore and Meara is an extremely delicate instrument.

One of the most complete instruments at present on the market is that of Frank and Petter. Recently, Frank has introduced a mirror-sphygmograph, in which a mirror is attached to the receiving pelotte, and a light-ray thrown upon this mirror is reflected upon a photographic registering apparatus.

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(b) *The Plethysmograph; Volume Pulse*

This is used but little clinically. The periodic dilatation of the arteries causes a rhythmical variation in the volume of the arm. With the plethysmograph, this variation is recorded in the form of a curve, called a plethysmogram.

The apparatus consists of a cylinder for receiving one upper extremity. The space in the cylinder between it and the arm is filled with water or air and the pulsations due to changes in volume are transmitted by means of a tambour and lever to a revolving drum. The tracing gives us information regarding the volume of the pulse and the readings are absolute when the apparatus is so calibrated that 1 mm. of ordinate in the tracing corresponds to a definite number of cubic millimeters (or centimeters) of increase in volume.

Morawitz (1907) applied it to determine the amount of blood present in the arm included in the instrument, and tried to draw deductions therefrom as to the total amount of blood in the body. Weber has used the plethysmograph to study the volume-changes accompanying psychic processes.

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(c) *The Tachograph; Velocity Pulse*

The speed with which the volume of an arm changes can be roughly measured by a tachograph (v. Kries; Frank). A little illuminating gas is allowed to pass through a chamber surrounding an arm and is lighted. As the arm increases in volume, the flame rises; as it decreases in volume, the flame falls. The alterations in the height of the flame are greater when the volume-change is rapid. By photographic registration of the flame on bromide paper, a curve known as a tachogram is obtained, which represents the rhythmical alterations of the velocity of the blood flow in the arteries (assuming that the current velocity in the veins is constant).

By registering simultaneously changes in current velocity and blood pressure, conclusions can be drawn as to alterations in the force of the heart. If the changes in pressure and in velocity are in opposite directions the cause is to be sought in changes in the peripheral resistance; the plethysmogram may then be used as a control.

T. G. Brodie has used a special method for estimating the blood flow in an organ. He suddenly occludes its efferent vein and measures the change of volume of the organ by an oncometer. The arterial blood enters without diminished speed at first, but the flow is soon retarded, owing to the rise of pressure in the veins and capillaries; thus the organ swells rapidly at first, and afterwards progressively more slowly. The early portion of the curve is said to represent the rate at which the blood enters under normal conditions. Hewlett and Van Zwaluwenburg have applied Brodie's principle to determine the rate of flow in the arm of man. They apply a distensible cuff similar to that used for determining arterial pressure and then try to adjust the pressure in the cuff so that the veins shall be occluded while the arteries are left open. They record the resultant changes in the volume of the arm by means of a plethysmograph and a Brodie volume-recorder.

Stewart (1911) has worked out a method that permits the quantity of blood passing through a part like the hand to be easily determined with approximate accuracy. The method is based upon the fact that the amount of heat produced by a part like the hand during rest is negligible in comparison with the heat conveyed to it by the arterial blood. The amount of heat given off by the hand to a calorimeter in a given time is determined and also the temperature of the incoming (arterial) and of the outgoing (venous) blood. From the data thus secured the amount of blood that must have passed through the hand to give off this amount of heat can be calculated.

The method for the measurement of the flow in the hands has also been modified by Stewart to apply to the feet, thus making it possible to secure observations on persons too ill to sit in a chair for hand-flow measurements.

Stewart has made careful studies of the blood flow in several forms of anemia, in fever, in diseases of the heart, in arteriosclerosis and thoracic aneurism, in peripheral neuritis, in hemiplegia, in certain pulmonary diseases, and in Graves's disease. The results are summarized in his lecture before the Harvey Society of New York (1912).

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(*d*) *Röntgenoscopy and Cinematography of the Movements of the Heart and the Aorta*

Besides the important information afforded concerning the form and position of the cardiovascular shadow, röntgenoscopy also yields us interesting data regarding the movements and pulsations of the great vessels and the several heart chambers. With each systole of the normal heart one can see a shrinking in the region of the lower left lateral curve (contraction of the left ventricle) and often a bulging of the upper left lateral curve (expansion of the aorta). Occasionally, systolic expansion of the middle curve on the left can be made out (pulmonary artery in patent ductus Botalli and occasionally in mitral disease). In tricuspid insufficiency it is sometimes possible to see a systolic expansion of the lower right curve due to reflux of blood into the right atrium on ventricular systole. Ventricular extrasystoles can also be observed fluoroscopically. The beginner should practice on bradycardiac patients, as the longer interval between systoles makes the observation easier.

Great practical importance in diagnosis accrues to röntgenoscopic examination of the movements of the walls of the aorta in aneurism (*q. v.*).

Cinematographic röntgenograms of the heart movements have been made but as yet have not attained to clinical importance.

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(*e*) *The Electrocardiograph*

As has long been known, the excited part of a strip of muscle behaves electronegatively toward the unexcited part. If an excitation extends along a muscle from one end to the other, each part becomes successively electronegative as the wave of excitation passes over it. Thus, if a beating heart be connected with a galvanometer, and the deflections of the needle be photographed, a curve known as an electrocardiogram is obtained. Waller showed that the action currents could be led off

Fig. 212.—Distribution of Cardiac Electricity on the Surface of the Body. (After A. D. Waller.)

from the human heart by applying electrodes to the extremities, those arising at the base of the heart being led off from the right arm, those from the apex from the left arm or the left leg. Waller used the rather sluggish capillary electrometer. A great step forward was made when Einthoven devised his delicate string galvanometer. The early heart stations were equipped with Edelmann's construction of the Einthoven apparatus. Recently, the convenient Cambridge electrocardiograph has come into vogue.

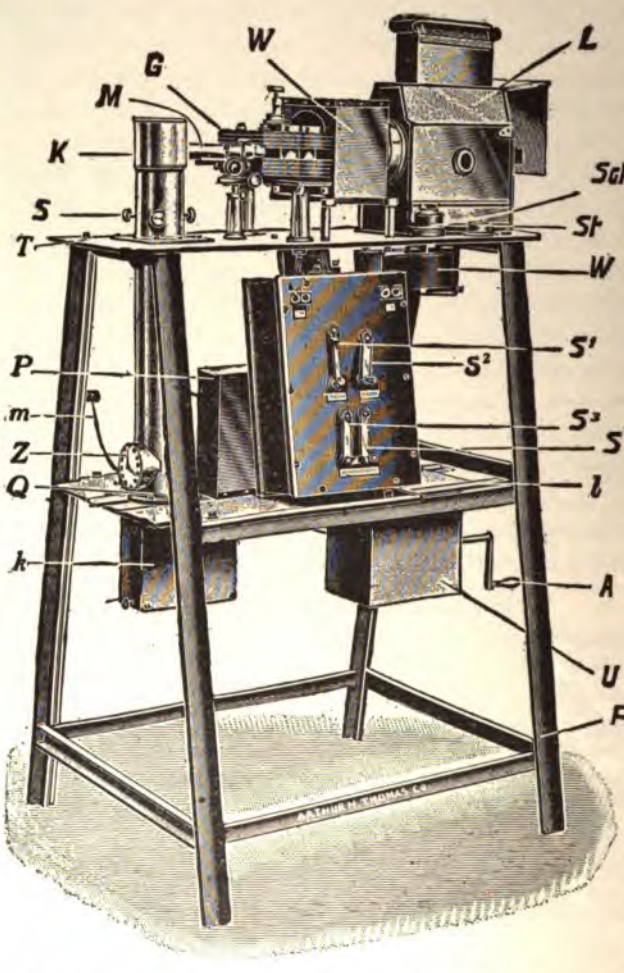

Fig. 213.—Small Electrocardiograph, Edelmann Model. New Simplified Electrocardiographic Outfit, Complete with L Arc Lamp, G Einthoven String Galvanometer with Permanent Magnet, M Projection Microscope, S^1 S^2 S^3 and S^4 Electric Devices for Determining the Sensibility of the Galvanometer and for Compensation of Skin Currents, Photographic Register, Electrodes and Stand. This Outfit is One of the Latest and Lowest Priced Complete Installations for the Taking of Electrocardiograms. (By courtesy of A. H. Thomas Co., Philadelphia.)

Dr. H. B. Williams of New York has recently designed an instrument similar in character to the original Einthoven instrument, but the outfit as a whole is less expensive. It is accurate, convenient of manipulation, and is provided with all necessary adjustments, including focusing fine adjustments and accurate centering devices for both microscopes, micrometer centering arrangements for the upper and lower ends of the string and a very fine micrometer for adjusting the tension of the string. The string can be easily adjusted so that it can be tightened and loosened over the entire working range without material change of focus or zero. The deflections are proportional to the strength of current for 8 cm. either side of zero at the usual magnification of 90

diameters. The lenses are made by the Spencer Lens Company of Buffalo, the projection lens being a 4 mm. apochromatic. The entire instrument is so rigid as to be but little affected by external vibrations and for clinical purposes it can

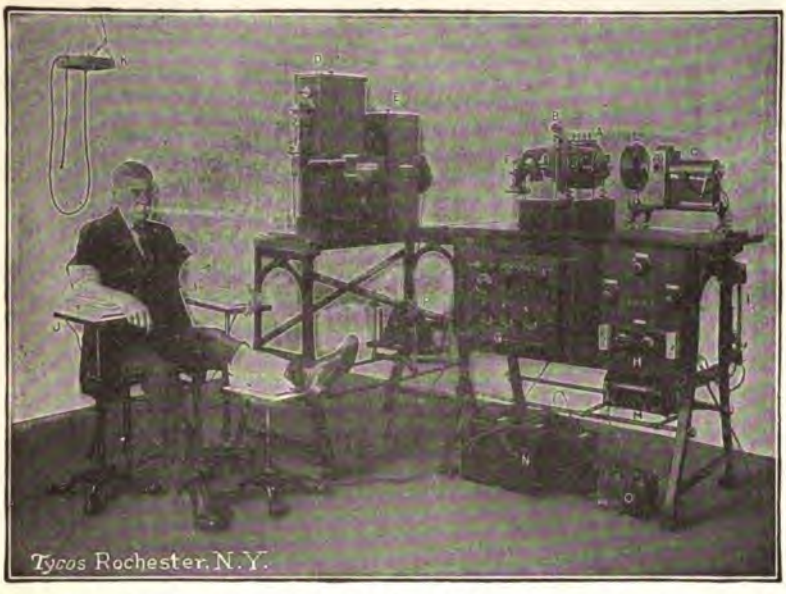

Fig. 214.—Large Electrocardiograph, Cambridge Model. (A) The Einthoven String Galvanometer Consists of a Fine Silvered Glass Fiber, Suspended Between the Poles of a Powerful Electromagnet. This Fiber or "String" Moves in Response to the Minute Currents Generated by the Action of the Heart; (B) the Camera Photographically Records the Magnified Movements of the Fiber; (C) the Automatic Arc Lamp Produces the Shadow (which is Photographed) of the Fiber; (D) the Control Board Facilitates the Making of the Necessary Tests and Connections; (E) the Time-marker Automatically Marks the Time Intervals on the Record; (F) the Electrodes by which the Patient is Connected to the Instrument; the Switchboard (G) Carries all Power Switches and Connections. (By courtesy of Taylor Instrument Co., Rochester, N. Y.)

be placed upon a solid wooden table in any reasonably substantial building. The weight of the apparatus is about 180 pounds. It is made by the mechanician, C. F. Hindle of Elmhurst, N. Y.

The resistance box arrangements for use with the instrument are made by Leeds and Northrup of Philadelphia after suggestions made by Dr. Williams. The whole outfit will be described in detail in the American Journal of Physiology. I am indebted to Dr. H. B. Williams for advance information regarding it. It is gratifying that a really satisfactory apparatus is now made in this country.

In these instruments, the movements of the string are magnified and projected through a slit upon a moving photographic film or plate. The electrocardiogram thus obtained is remarkably constant in health. In diseased conditions, striking deviations from the normal curve may be obtained, and they have proved to be valuable for diagnosis.

The technic, though complicated, can easily be learned in a properly equipped heart station. For the details, my paper on electrocardiography and electrophonography may be consulted.

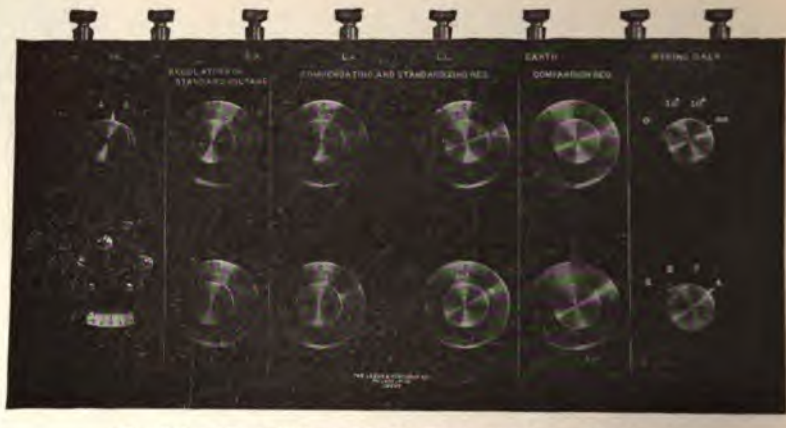

Fig. 215.—The Williams-Hindle Electrocardiographic Outfit.
(By courtesy of Dr. H. B. Williams.)

Several modes of leading off the current are used. For clinical purposes, three leads suffice. These are known as:

Lead (or *Derivation*) *I* = Right arm and left arm.
Lead (or *Derivation*) *II* = Right arm and left leg.
Lead (or *Derivation*) *III* = Left arm and left leg.

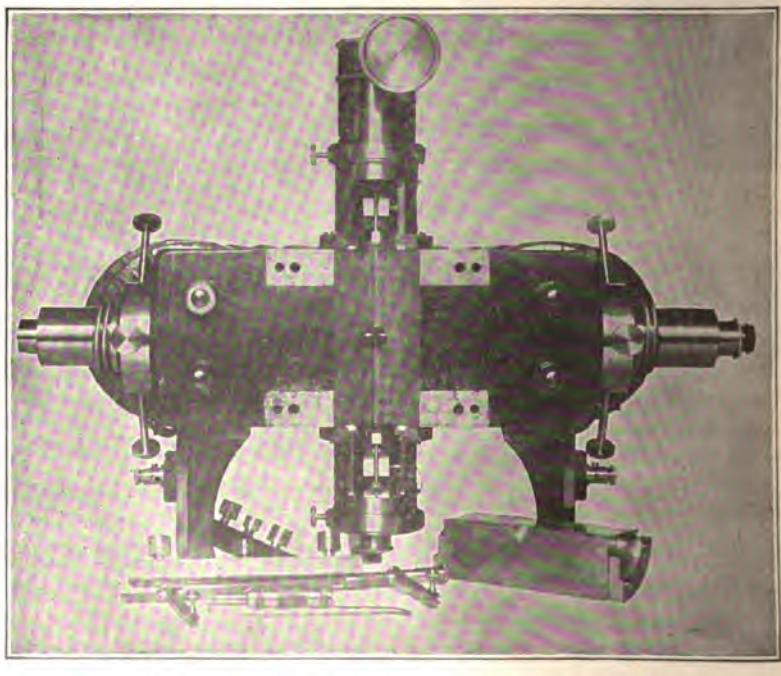

Fig. 215a.—The Williams-Hindle Electrocardiographic Outfit.
(By courtesy of Dr. H. B. Williams.)

Since the form of the electrocardiogram is to some extent affected by the posture of the body, it is desirable to examine patients always in one

Fig. 215b.—The Williams-Hindle Electrocardiographic Outfit.
(By courtesy of Dr. H. B. Williams.)

position, say the recumbent posture. A description of the normal and of pathological electrocardiograms will be given farther on.

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E. Analysis of the Movements of the Heart and Vessels as Studied Clinically

We may now pass to an analysis of the several movements the study of which may be helpful in clinical diagnosis.

1. The Apex Beat of the Heart

The determination of the position of this has already been discussed. The features of the apex beat that we are concerned with here include: (a) The extent of the beat; (b) its strength; (c) its resistance to compression; (d) its exact form and the relations of the details of this to happenings within the heart and vessels; and (e) its rhythm.

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(*a*) *The Extent of the Apex Beat*

In extent, the area of the apex beat varies greatly both in health and in disease. In some instances no apex beat is visible or palpable. Usually, in health, it occupies an area 10 to 15 mm. in diameter, but anything that excites the heart (emotion, sudden change of posture, exertion) will give rise to a more diffuse pulsation.

Temporary changes in extent of the apex beat are of but little clinical significance, but a permanent enlargement of the area indicates hypertrophy or dilatation of the left or of the right ventricle or of both.

When the left ventricle alone is enlarged, as in some cases of aortic insufficiency, the apex beat may be tolerably well circumscribed, presenting a rounded elevation resembling a segment of a small sphere (*choc en dome*). When this domelike impulse coexists with enlargement of the heart, as revealed by percussion, and with throbbing ar[illegible] celer), it is pathognomonic of aortic insufficiency, even in th[illegible] diastolic murmur (Bard).

A more diffuse shock is met with when both ventricles [illegible] phied and dilated (renal heart, chronic alcoholism, arterio[illegible] forms of valvular disease). The area is larger and the ele[illegible] what elongated, resembling the curve of an upturned boat, [illegible] a cathedral (*choc globuleux* of Bard).

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(*b*) The Strength of the Apex Beat

The *strength* of the apex beat, as felt by the palpating hand, also varies within wide limits. An enfeebled apex beat does not always indicate disease of the heart; it may depend upon pulmonary emphysema, or upon obesity. Only when in the course of observation an apex beat that has been strong is noticed to grow weaker, is it an indication of enfeeblement of the heart muscle accompanying dilatation. Thus, in acute infectious diseases, particularly in acute rheumatism, such a change should make one suspect the development of a cardiac complication.

The apex beat may be feeble, even when the heart is hypertrophied and the blood pressure high, as in some cases of contracted kidney and arteriosclerosis. In this case, the feeble heart may point to a failing heart-muscle.

The energy of the apex beat is often apparently increased in fevers when the contractions of the heart are really less vigorous than normal. This apparent increase in energy is probably due to the abruptness and brevity of the weakened ventricular systoles. Contractions of the heart that give rise to what seem to be violent apex beats have often little effect upon the blood pressure, as one can readily observe in paroxysmal tachycardia.

(*c*) The Resistance of the Apex Beat to Compression

The *resistance of the apex beat to compression* is a better guide to the vigor of the contracting heart than is the apparent energy of the beat itself. The hypertrophied left ventricle in aortic insufficiency gives rise to an apex beat (*choc en dome*), mentioned above, which is markedly resistant to the pressure of the palpating hand. The determination of the resistance of the apex beat to compression is therefore of considerable diagnostic importance.

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(*d*) The Exact Form of the Apex Beat as Revealed in the Cardiogram

The *exact form* of the elevation known as the apex beat and the relations of the details of this to the happenings within the heart itself can be studied best with the aid of graphic records.

Graphic curves of the apex beat, *cardiograms*, can be secured by the use of Jaquet's cardiosphygmograph or of Mackenzie's polygraph. A cardiogram represents partly a pressure curve and partly a volume curve, for changes in volume as well as changes in pressure of the heart during systole will modify the curve. Of all sphygmographic curves, the cardiogram is the most difficult satisfactorily to interpret. Clinicians have accordingly made but relatively little use of it.

The ordinary form of curve obtained is a *trapeze*. Often there is a small wave (due to atrial contraction) just preceding the main elevation. Sometimes this is fused with the ascending limb of the main elevation, in which event the curve rises almost perpendicularly to its height, then falls a little, after which a plateau is formed, followed by an almost perpendicular fall of the descending limb.

A second form of cardiogram, by no means uncommon, is the *jerking*, or *quickly rebounding, type*, in which the ascending and descending limbs of the curve form the two sides of a triangle.

In making a cardiogram of the apex beat, care should be taken to distinguish between the true apex formed by the left ventricle and elevations medial therefrom due to the right ventricle. A comparison of the cardiogram with a simultaneous arteriogram of the carotid artery makes analysis much easier. The ascending limb of the cardiogram corresponds

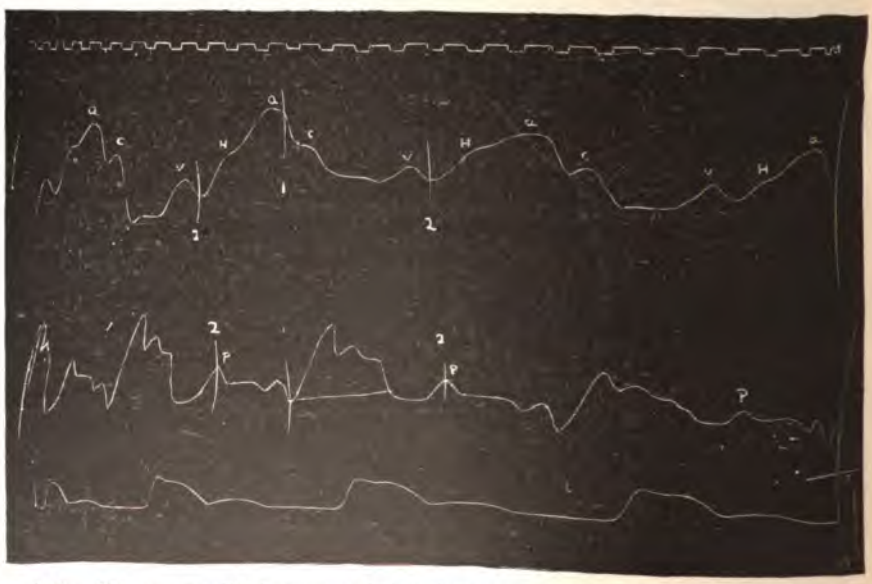

Fig. 216.—Cardiogram, Phlebogram and Arteriogram in a Person Presenting a Third Heart Sound (Protodiastolic Gallop). Normal Heart. The Upper Tracing is from the Jugular Vein; the Middle Tracing is the Apex-cardiogram; the Lowest Tracing is from the Brachial Artery. The Time Registers Tenths of Seconds. The Third Heart Sound Occurs at the Point Marked "2" in the Tracings; this Corresponds to the Foot of the *h* Wave in the Phlebogram and to the Protodiastolic Wavelet *P* in the Cardiogram. (After W. S. Thayer, Arch. Int. Med.)

to the closure-time or tension-time, that is, to the period in which all the heart valves are closed (first phase of systole). The beginning of the expulsion-time of systole is indicated in the carotid arteriogram by its ascending limb, while in the cardiogram the expulsion-time of systole corresponds to the plateau and to a part of the descending limb of the curve. The second sound of the heart, corresponding to the end of systole, occurs during the descending limb of the cardiogram; thereafter the curve falls rapidly to the abscissa. Sometimes, during diastole, the curve falls below the abscissa, corresponding to slight diastolic retraction in the apex region.

Systolic retraction of the apex is shown as a *negative cardiogram*, that is to say, the curve is reversed, falling below the abscissa instead of forming an elevation above it. Thus in mediastinopericarditis the systolic retraction yields a cardiogram in which the curve during the whole of systole lies below the abscissa. A similar curve can, in normal cases, be obtained over pulsations of the chest wall caused by the right ventricle.

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Esophageal Cardiogram (Frédéricq, Minkowski).—The graduated stomach tube is covered at its end by a fine rubber balloon 4 cm. long. The tube is introduced into the stomach, after which the balloon is distended by blowing air into it. It is then withdrawn through the cardiac end of the stomach into the esophagus. The outer end of the tube is connected by a T-shaped tube with a Marey tambour and with an inflating bulb. By slowly withdrawing the tube, the site will be found where pulsations of the left atrium are maximal (7-9 cm. above the cardiac orifice of the stomach). The patient holds his breath, and the curve is recorded, the pressure within the tube being kept low (30 mm. water). It is well to record simultaneously a phlebogram of the jugular vein, and an arteriogram of the carotid artery.

The esophageal cardiogram permits one to recognize paralysis of the left atrium and allows of a study of the behavior of the left atrium in the cardiac arhythmias.

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(*e*) *The Rate and Rhythm of the Apex Beat*

The palpation of the apex beat further reveals the variati
and *rhythm* to which the contractions of the left ventricle a
The palpating hand can recognize the existence of rapid ac
heart (*tachycardia*), of slowed action (*bradycardia*), of many
of disturbed rhythm (*arhythmia*), and sometimes of gallop rl

Most of these disturbances of rhythm are better studied, however, by means of the analysis that arteriograms, phlebograms and electrocardiograms permit.

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2. Precordial Movements Other than the Apex Beat

Besides the apex beat, certain other pulsations over and near the heart should be looked for. On inspection in pathological states one may see: (a) wavelike movements over the right ventricle; (b) retractions at the base or apex; or (c) pulsations over the aorta or pulmonary artery. On palpation, these various movements may be felt, and in addition the palpating hand may perceive (d) certain shocks due to closure of valves, (e) certain thrills, the palpatory equivalent of some kinds of murmurs, or (f) friction fremitus, the palpatory equivalent of the pericardial friction rub heard on auscultation.

(*a*) *Wavelike Movements in the Precordium*

In young, thin people and even in adults, during excitement, or on exertion, slight visible movements can often be made out in the third, fourth and fifth intercostal spaces to the left of the sternum. When marked, and especially in the adult, they often indicate either hypertrophy of the right ventricle or an adherent pericardium. They are also sometimes seen when the heart is not diseased, owing to retraction of the lung and consequent approximation of a larger surface of the heart to the chest wall. A marked *palpable* pulsation over the lower part of the sternum or to either side of it is usually due to a hypertrophied right ventricle.

(*b*) *Retractions at the Base and Apex*

In young, thin people with cardiac hypertrophy one can often make out a systolic retraction at the base of the heart at the level of the third and fourth interspaces. It is most marked in cases where there has been retraction of the borders of the lungs. It is of no special diagnostic significance.

More important is a systolic retraction visible and palpable at the apex. At the moment when the palpating hand feels the hardening of the apex one can see a depression synchronous with the systole, and the cardiographic tracing reveals this still more distinctly (see above). The retraction may be limited to one or may involve several intercostal spaces. Two conditions must be considered:

1. Adherent pericardium (mediastinopericarditis) with enlargement of the heart, and

2. Enlargement of the right ventricle so that the apex of the heart is formed by this rather than by the left ventricle. A cardiogram taken over the right ventricle always shows systolic depression, that over the normal apex beat (left ventricle) shows systolic elevation (see above).

The meaning of the sign can be decided only with the aid of other methods of examination.

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(*c*) *Pulsations Over the Aorta and the Pulmonary Artery*

The aortic and pulmonary areas should always be carefully inspected. A pulsation in either region usually indicates a dilatation of the underlying artery. Such a dilatation may be dynamic or it may be due to aneurism. Aneurism of the ascending and transverse portion of the arch of the aorta often causes a pulsation in the second and third spaces on the right side, or the whole upper part of the sternu elevated. The pulsations are almost synchronous with the Many an aortic aneurism is missed because the examiner has undress his patient and to view the chest carefully in pr the aneurism is large an actual pulsating tumor may be see hand feels not only an elevation but also a characteristic *ex* the mass.

Not infrequently there is visible pulsation in the pulmonic area (second intercostal space on the left, close to the sternum). This may be of no significance, though sometimes it indicates a dilatation of the pulmonary artery and is occasionally associated with pulmonary stenosis. Now and then the pulsation seen here may be due to marked activity in the auricular appendix of the left atrium. A faint systolic pulsation at the sternal ends of the second, third and fourth left interspaces that is due to the expansion of the internal mammary artery, which underlies the thoracic wall in this situation, is not infrequently seen.

(*d*) *Shocks Due to Valve Closure*

If one palpate over the areas designated as "auscultation sites" for the four main orifices of the heart, the hand will sometimes feel a vibratory shock, the tactile equivalent of the valvular component of the heart sounds, due to the tension of the valves. In normal hearts, these shocks are scarcely perceptible, but in certain diseased states they may become pronounced and be valuable aids in diagnosis; the local conditions most often responsible are abrupt closure of valves, sudden tension, or thickened valves.

An exaggerated mitral valve shock is best felt over the apex. It is most marked in mitral stenosis as an abrupt shock immediately succeeding the presystolic thrill (*dureté clôturale* of L. Bard). This sign may suffice for the making of a diagnosis of mitral stenosis when the arhythmia or tachycardia are so great as to interfere with the production, or the perception, of the characteristic audible signs of mitral stenosis.

An exaggerated vibratory shock, transmitted from the semilunar valves of the aorta, is sometimes felt in the second or third intercostal space to the right of the sternum in arterial hypertension, especially when associated with arteriosclerotic thickening of the valves.

An exaggerated tricuspid valve shock, palpable over the xiphoid, is rarely felt, as tricuspid stenosis is an uncommon affection.

Exaggerated shock over the pulmonary area is a very common palpatory phenomenon met with in the various conditions that increase the pressure in the pulmonary artery (mitral disease, emphysema, pulmonary arteriosclerosis, fibroid phthisis).

Corresponding to the doubling of the second sound, audible when the pulmonary and aortic valves do not close simultaneously, a double vibratory shock can sometimes be felt.

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(e) *Certain Thrills, the Palpatory Equivalent of Some Kinds of Murmurs*

The liquid veins that give rise to vibrations that, on auscultation, are recognizable as murmurs or rumbles, can sometimes be felt, on palpation, as *thrills.* The sensation perceived by the hand reminded Laennec of that obtained on stroking a purring cat.

The liquid veins that cause slow vibrations yielding low-pitched murmurs are the ones that favor the formation of thrills, whereas those that yield rapid vibrations producing high-pitched murmurs may not give rise to palpable thrills. This explains why a thrill may sometimes be felt when a murmur is not audible or is a very indistinct rumble and why the loudest and most distinct blowing murmurs may be unaccompanied by thrills. Palpation and auscultation here supplement one another advantageously in diagnosis.

Thrills are best felt during expiration and when the heart rate is somewhat accelerated. The most distinctive thrill is that which accompanies mitral stenosis. Like the murmur due to this lesion, it may be perceptible only in the presystole, or it may occupy a longer period of diastole. It is usually maximal a little above and just medial from the apex beat, in the exact situation in which mitral stenotic murmurs are usually best heard. It is important to time this thrill exactly in order not to confuse it with the systolic thrill that accompanies mitral insufficiency. The purring thrill of mitral stenosis terminates abruptly with the exaggerated mitral valve shock at the beginning of the first sound; the systolic thrill of mitral insufficiency begins only with this shock and follows it into systole.

A systolic thrill, maximal in the aortic area and propagated upward, is more important than a systolic murmur in the same area for the diagnosis of aortic stenosis. A thrill in the same area is sometimes palpable over the expansile pulsation of an aortic aneurism. Diastolic aortic thrills are occasionally met with, but are rare. When present they are felt along the left margin of the sternum.

In tricuspid stenosis, a diastolic, or a presystolic, thrill may be felt over the tricuspid auscultation site.

A systolic thrill in the pulmonary area, propagated toward the left clavicle, often accompanies stenosis of the pulmonary orifice. A systolic thrill in the same region or a little lower down, propagat
a transverse rather than in an upward direction, is met wi
interventricular septum.

From what has been said it is obvious that *the palpa*
more commonly met with and more helpful in the dia
of the mitral and aortic orifices than in other conditio
rarely in association with valvular insufficiencies. T

well to practice the appreciation of thrills at every opportunity that offers, as nowhere else in diagnosis is the *tactus eruditus* more helpful.

(*f*) *Pericardial Friction Fremitus*

This is the palpatory equivalent of the friction rub audible on auscultation and due to dry pericarditis. To the hand, it feels very superficial and differs from pleuritic friction (1) in its rhythm and (2) in the fact that it can be felt when the patient holds his breath. Occasionally, pericardial friction fremitus is very easily perceptible, but the rubs are often too delicate to yield tactile sensation and auscultation is, therefore, more helpful than palpation in the diagnosis of pericarditis.

3. Broadbent's Sign and Other Pulsations in the Back

In cardiac cases, the back and sides, as well as the front, of the thorax, should be inspected. In adherent pericardium, there may often be observed a *systolic retraction* of one or more ribs in an area a little below and lateral from the angle of the scapula on the left side, persisting when the patient holds his breath (*Broadbent's sign*).

While inspecting the back, one should also ascertain the presence or absence of *pulsation in the left interscapular space,* as occasionally an aneurism of the thoracic aorta presents here. In one instance, I observed a pulsating angiosarcoma presenting in this region.

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4. Abdominal Pulsations

The abdomen should be carefully examined for the presence of epigastric, abdominal or hepatic pulsations.

(*a*) *Epigastric Pulsation*

By this is meant pulsation in the epigastric fossa, in the neighborhood of the xiphoid process between the two costal margins, due directly or

indirectly to the heart. It may depend upon (a) the abdominal aorta, or (b) the right ventricle.

The most *common aortic form* is that met with in neurasthenics and emaciated dyspeptics with thin, loose abdominal walls ("dynamic aorta"). This pulsation is slightly to the left of the middle line and extends for a variable distance downward, below the xiphoid process. The pulsation is perpendicular from behind forward, has only a slight breadth and is somewhat later than the apex beat. One tone, or a systolic murmur, may be audible on auscultation. The pulsation is increased by anything that excites the heart's activity. The tyro is only too prone to think of the existence of aortic aneurism in his earlier experiences with this comparatively insignificant form of epigastric pulsation. In many cases in which this form of aortic pulsation is present the aorta can be grasped in the palpating hand, which then becomes aware of marked lateral expansion with each pulsation. In such cases, however, the aorta can be palpated lower down and the same condition found to be present there; there is never a localized *expansile tumor* such as is present in aneurism of the abdominal aorta.

In *aneurism of the abdominal aorta* the pulsation is more powerful and a definite tumor is distinctly expansile in all directions, a fact that helps to distinguish aneurism from propagated aortic pulsations due to intervening fecal masses or neoplasms. Abdominal aneurism is usually accompanied by severe pain.

Epigastric pulsations due to the right ventricle itself may be either systolic elevations or systolic retractions. *Systolic elevations* are usually due to a lowered and enlarged right ventricle (pulmonary emphysema, dilated right heart, cardioptosis).

Systolic retractions in the epigastrium, due to the right ventricle, are rather diffuse, wavelike movements depending upon elevation of the diaphragm by the contracting right ventricle; they are of no clinical significance.

(*b*) *Hepatic Pulsation*

This is best made out by palpation. When the right heart begins to fail, the liver usually enlarges from chronic passive congestion and its lower edge can be made out on palpation. Sometimes this enla can be felt to pulsate, though the details of the pulsation ca discerned by graphic registration. The curve shows a systolic approximately synchronous with that of the apex beat; it is *tricuspid insufficiency,* to a wave propagated through the vena ca from the right heart. A presystolic wave on the hepatic pulse with the atrial contraction, is occasionally met with in *tri* (J. Mackenzie).

5. Pulse in Arteries, Veins and Capillaries

The pulsations due to *aneurisms of the aorta* have already been referred to. Aneurisms may occasionally be seen and felt in other arteries of the body.

On inspecting the thorax for pulsations and anomalies, a *superficial internal mammary artery* is occasionally met with pulsating in the second and third intercostal space, but is easily recognized. When many dilated, tortuous arteries are seen pulsating over the thorax without apparent cause one should think of a *narrowing of the arch of the aorta.*

Markedly *throbbing carotids* are highly characteristic of aortic insufficiency, though one occasionally sees similar throbbing in Graves's disease and other states.

Pulsation in the jugular fossa from below upward may indicate either a high position of the arch of the aorta or dilatation thereof.

Pulsations in the veins of the neck may be visible in health, though they are much more often seen in disease. A *normal venous pulse* when visible presents two waves recognizable by the eye, one diastolic, the other presystolic in time. In *tricuspid insufficiency* a single large wave is visible, systolic in time. For the finer details of the venous pulse, graphic registration is essential. Palpation is of little value in the study of the venous pulse.

In heart block, inspection of the jugular pulse combined with auscultation or palpation at the apex will often suffice to show that the atria (or auricles) are contracting at a more rapid rate than the ventricles.

Visible pulsation of the peripheral arteries occurs also in aortic insufficiency. For the characters of the arterial pulse, however, we rely mainly upon palpation and upon graphic registration.

A *visible capillary pulse* is met with in conditions associated with hypertrophy of the left ventricle, especially in aortic insufficiency. If one scratches a line with the finger nail on the forehead or skin of the trunk, or presses slightly upon the end of the patient's finger nail in order to make a pale spot in the nail bed, the borders of which may be closely watched, one can see alternately blush and pallor if a capillary pulse exists. A very good way to look for a capillary pulse is to press gently with a glass slide on the lips. Sometimes a blush of the cheek can be seen with each systole of the heart.

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(*a*) *Value of Studies of the Pulse*

The movements of the blood wave in the arteries and veins permit us to draw conclusions regarding the activities of the muscular walls of the

left ventricle and of those of the right atrium respectively. The activity of the left atrium can be registered, as has been seen, by means of a tube introduced into the esophagus. We get some clews to the movements of the right ventricle by registering the movements in the third and fourth intercostal space on the left side and by a study of the venous pulse, since some of the movements of this ventricle are transmitted to the blood in the veins.

(*b*) *Arterial Pulse*

The arterial pulse is studied clinically (1) by palpation, and (2) by sphygmography.

i. Palpation of the Arterial Pulse

In ordinary clinical work the radial artery is felt with the tips of the second, third and fourth fingers applied to the wrist, where the vessel can be easily pressed against the underlying radius. By pulse one means the pressure wave of enlargement of the artery that occurs at each systole of the heart and which takes a perceptible time to travel from the heart to the periphery. One pays attention to seven qualities: (1) the frequency; (2) the rhythm; (3) the volume; (4) the quickness or celerity; (5) the tension; (6) the fullness; and (7) the equality on the two sides of the body.

The thickness of the vessel, which is usually attended to at the same time, is not a pulse phenomenon, but has to do with the condition of the arterial wall itself.

1. **Frequency of the Pulse** (*Pulsus frequens et rarus*).—This varies in healthy adults between 60 and 80 beats per minute (average 72); in children 90 to 140; in old age 70 to 90. The pulse is faster in women than in men. On sitting or on lying, the pulse is slower than on standing or on exercising.

Acceleration of the pulse rate is known as *pulsus frequens;* it is due to heart hurry or TACHYCARDIA. It is met with normally on exertion, during emotion, and after taking food. In fever, for each degree centigrade the temperature is raised above 37° C., there is ordinarily an increase in the pulse frequency of about eight beats per minute; exceptions to this rule, are, however, met with in typhoid fever, where the acceleration is much less, and in scarlet fever and diphtheria, where
greater.

In vagus paralysis, in Graves's disease, and in
states, tachycardia is common. A frequent pulse is often
of cardiac weakness or collapse. In paroxysmal ta
great frequency of rate having a sudden onset, and o
met with, alternating with periods of normal frequen

last from a few minutes to several days, the pulse beats often numbering between 140 and 280 per minute.

A tachycardia, with regular pulse, that persists for months and is not due to Graves's disease, the arterial pulse rate remaining above 120, especially if it occurs in an elderly person, is most often due to atrial (or auricular) flutter. The venous pulse then usually has a rate double that of the arterial pulse. This condition will be described further on.

Slowing of the pulse rate is known as *pulsus rarus* or BRADYCARDIA. It is met with in convalescence from many infectious diseases, especially typhoid and pneumonia, in disturbances of digestion, in conditions in which the vagus centers are stimulated (brain tumors, hydrocephalus, beginning meningitis), in icterus and in various diseases that affect the heart itself (aortic stenosis, coronary sclerosis, myocarditis). In Stokes-Adams syndrome, where the stimulus from the sinus and auricles is prevented from reaching the ventricles, the latter contract in their own independent rhythm; in these cases the arterial pulse rate may fall below thirty.

A bradycardia arising in the heart itself, either as a result of diminished stimulus-formation, or of slowed or interrupted stimulus-conduction, can be distinguished from one due to vagus stimulation by the subcutaneous injection of 0.001 gram of atropin. Vagal bradycardias disappear under atropin since this drug paralyzes the terminations of the nerve and so removes its inhibitory effect.

2. **Rhythm of the Pulse** (*Pulsus regularis et irregularis*).—Normally, the single pulse waves follow one another regularly (*pulsus regularis*), but in pathological conditions the rhythm may become irregular (*pulsus irregularis*). The irregular pulse is due to cardiac arhythmia. Under this heading we shall have to study (1) respiratory irregularities, (2) extrasystolic irregularities, (3) heart block, (4) perpetual arhythmia, and (5) the alternating pulse. The subject will be dealt with more fully further on.

3. **Volume of the Pulse** (*Pulsus magnus et parvus*).—What clinicians speak of as the volume of the pulse is dependent chiefly upon the difference between the increase in pressure during arterial diastole (ventricular systole) and the decrease in pressure during arterial systole (ventricular diastole). The size of the pulse waves depends chiefly upon (1) the volume of the systolic output of the left ventricle; and (2) the ease with which blood flows out of the arteries through the capillaries. The volume of the pulse is, therefore, the palpatory equivalent in the radial artery of what is known as the pulse pressure (difference between maximal systolic and minimal diastolic pressure). The latter can now be very accurately measured (*q. v.*).

When the volume of the pulse is large it is spoken of as a *pulsus magnus* (aortic insufficiency, renal cardiopathy); when the volume is small we

speak of a *pulsus parvus* (aortic stenosis, some cases of myocardial insufficiency, syncope).

4. **Quickness, or Celerity, of the Pulse** (*Pulsus celer* and *Pulsus tardus.*)—By celerity is meant the time taken for the widening and subsequent contraction of the arterial tube. If the pulse wave rises very quickly and falls rapidly, it is spoken of as a *pulsus celer* (Corrigan pulse). If, on the other hand, the artery expands slowly and also collapses slowly, we speak of a *pulsus tardus.* The greater the systolic output and the lower the minimal blood pressure depending on lowered peripheral resistance, the greater, as a rule, the celerity of the pulse. The most outspoken pulsus celer is met with in aortic insufficiency, whereas the pulse in aortic stenosis is a good example of pulsus tardus. The pulsus celer is sometimes spoken of as the "water-hammer pulse."

5. **Tension of the Pulse** (*Pulsus durus* and *Pulsus mollis*).—This refers to the degree of tension (not thickening nor hardening) of the wall of the artery; on palpation it is judged by the force required to obliterate the pulse when the fingers press upon it. Three fingers are placed upon the radial; one presses with the most distal of these hard enough to prevent a recurrent pulse wave through the palmar arch; pressure is then made with the most proximal finger until the pulse ceases to be perceptible to the finger in the middle. If difficult to compress, the pulse is said to be of high tension (*P. durus*); when easily compressible it is of low tension (*P. mollis*). Even skilled observers are sometimes wrong in their judgment as to the tension of the arterial wall, and it is better to rely upon objective measurements with the blood-pressure apparatus. What one attempts to measure here by palpation is the maximal systolic blood pressure.

A marked degree of *hypertension* is met with in contracted kidney, in lead colic, in the gastric crises of tabes, in pseudo-anginas, in other arterial crises, in some cases of arteriosclerosis, and in polycythaemia hypertonica. Marked *hypotension* is seen in Addison's disease, in fevers, in anaemias, in tuberculosis, and in some cases of failing heart.

One must distinguish between the tension of the pulse here described and thickening or sclerosis of the arterial wall. In the latter, if one obliterate the pulse with one finger and palpate the artery distal from the point of compression, the thickened vessel can be rolled between the finger and the bone. Instead of being smooth, straight and scarcely perceptible like a normal radial artery, it may feel thickened like a
the finger, elongated and tortuous. If the thickening
especially if the artery be calcified, a string of nodules v
neck artery).

6. **Fullness of the Pulse** (*Pulsus plenus et inanis*).—
of the pulse above described depends upon variations
the artery, the fullness of the pulse is a special conce

the mean state of filling of the artery. Either with constant pressure or with pressure-variations, the artery may in one case be large and full (*P. plenus*) and in another seem small and empty (*P. inanis*). To judge of the "mean filling" the observer must *pay attention to the volume of the collapsed artery between two pulses*, as well as to the size of the pulse wave. It is only the more marked deviations from the normal filling which can be recognized.

A *full pulse* is met with in healthy, strong men during and after muscular exertion, and often at the beginning of febrile diseases, whereas an *empty pulse* is encountered in anaemia, in cachexias, in chronic febrile diseases and in cardiac weakness. In aortic insufficiency the pulse feels full at the height of the wave but empty between two waves. The fullness of the pulse is, as a rule, but little regarded by clinicians, and, in my opinion, with right.

7. **Equality of the pulse in the two radials** as regards both time and altitude should be examined by palpation. The pulse at one wrist may appear slightly before the other, or the pulse wave may be higher in one radial than in the other. In either case we have to deal with a PULSUS DIFFERENS (*quoad tempus aut altitudinem*) due to the narrowing of the lumen of one of the arm arteries (congenital difference, tumors, aneurisms, etc.).

The most common cause of differences in the pulse in the two radials is the presence of an abnormally small radial artery on one side. This is a common anomaly in the arterial system of the forearm. As a result, the pulses vary chiefly in absolute volume: they are equal in time. In aneurism of the arch of the aorta, or of one of the arterial trunks supplying the arms, differences in the time as well as in the volume and tension of the two pulses are prominent.

ii. Graphic Registration of the Arterial Pulse (Sphygmography)

Curves or tracings of the arterial pulse **(arteriograms)** are obtained either with the polygraph of Mackenzie or the sphygmograph of Jaquet, referred to above. The tracing of each pulse beat presents an ascending limb and a descending limb. The *ascending limb* rises abruptly and corresponds to a very brief period; the *descending limb* falls slowly, covering a longer period of time. Secondary waves occur normally on

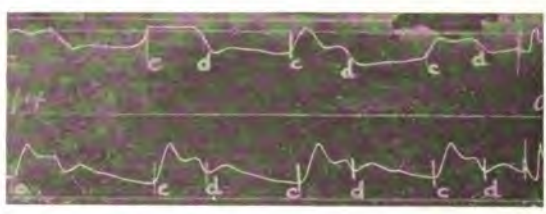

Fig. 217.—Carotid Arteriogram (Lower Tracing) with Cardiogram (Upper Tracing) for Comparison. (*c*) Time of Beginning of Anacrotic Limb of Arteriogram. (*d*) Time of Dicrotic Notch. (Personal Observation, J. H. H. Bull.)

the pulse increases, the depression preceding the dicrotic wave reaches a point as low as the beginning of the ascending limb (*complete dicrotic pulse*). When the pulse is very frequent, it may become *supradicrotic,* the depression preceding the dicrotic wave, then falling to a lower level than the beginning of the ascending limb preceding. In rare instances, the dicrotism is so extreme that the dicrotic wave becomes swallowed up in the ascending limb of the main wave (*monocrotic pulse*).

The arteriogram is of but little help in judging of blood pressure, though, where the mean blood pressure is high, a secondary anacrotic wave may appear before the apex of the main wave, and the dicrotic wave may become insignificant or may disappear.

The arteriogram is of greatest value in the analysis of cardiac irregularities and yields data indispensable for forming judgments regarding the activities of the left ventricle and their time relations. The arteriogram of the carotid pulse is much more helpful for these purposes than is that of the radial pulse; indeed, if one have good carotid arteriograms to compare with simultaneously recorded phlebograms and cardiograms, he may very well dispense with radial arteriograms.

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(c) *Venous Pulse*

The venous pulse is studied clinically (1) by inspection and palpation; and (2) by sphygmography.

i. Inspection and Palpation of the Venous Pulse

To inspect the venous pulse, the patient should be in a reclining position, the head and neck supported by a single pillow. If venous stasis be marked, the upright or sitting position may be better. A wave becomes visible when the intravenous exceeds the atmospheric pressure; a collapse becomes visible when the intravenous pressure is less than the atmospheric. If the intravenous pressure be continuously negative, or continuously positive, no venous pulse will be seen.

A pulse in the veins of the neck can be seen in a majority of healthy persons. This pulse is diffuse and wavy; as a rule, it cannot be felt by a palpating finger. An interesting feature of it lies in the fact that, on inspection, the collapse of the vessel is usually a more marked phenomenon than the positive impulse.

Under normal conditions, two pulsations occur in the vein for one in the artery; the collapse of the vein after the first pulsat
chronous with the arterial pulse, *i. e.,* it corresponds in time t
ular systole. This normal venous pulse is often referred to as
logical," "negative" or "double" venous pulse in contra
the "positive" or "single" venous pulse met with in tricuspi

After one has studied graphic tracings (see below), l
much more from simple inspection. Thus, if a normal

present, he can make out for each palpated pulsation of the carotid, two positive waves in the vein (*a*- and *v*-waves) and two collapses (*x*- and *y*-depressions).

Volhard has devised a simple instrument for determining the character of a venous pulse by inspection. For this he makes use of two U-shaped glass tubes, in each of which there is a colored fluid. To the open end of each tube is attached some rubber tubing and a small receiving funnel. One funnel is placed on the carotid and the other on the jugular bulb; the fluids are set into pulsation. If the two pulsations are in the same direction, the venous pulse is systolic or positive; if in the opposite direction, the venous pulse is presystolic or negative.

I would suggest that the student first familiarize himself with the graphic records as described below and, afterwards, take up the study of simple inspection and palpation of the veins of the neck.

ii. Graphic Registration of the Venous Pulse

The receiver of the registering apparatus is placed above the clavicle over the bulb of the jugular vein, preferably between the two heads of the sternocleidomastoid muscle. The patient should assume the position in which the venous pulse is best marked. As a rule, a reclining position with the head slightly elevated and turned to the left side is best, though various positions may have to be assumed before the optimal one is found. Occasionally, a better tracing can be secured by placing the receiver over the external jugular vein than over the internal jugular.

Tracings of the venous pulse, or *phlebograms,* are of but little value except in association with simultaneously recorded arteriograms and cardiograms, for only with these is it possible, in many cases, to refer the waves of the venous pulse to particular phases of the cardiac revolution.

The waves of the venous pulse are due to alterations in the blood pressure existing in the jugular vein and in the right atrium; the latter, in turn, are in part dependent upon the functions of the tricuspid valve

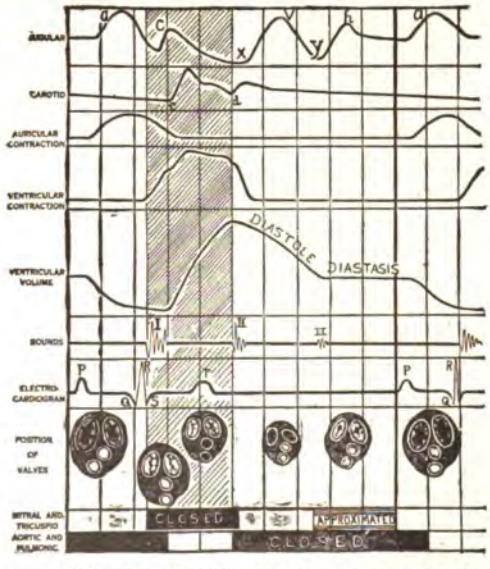

Fig. 219.—The Shaded Portion of the Cardiac Cycle Corresponds to Ventricular Systole. (From A. D. Hirschfelder, "Diseases of the Heart and Aorta," published by J. B. Lippincott Co., Philadelphia.)

and the activities of the right ventricle. Important conclusions can therefore be drawn from the venous pulse regarding the functions and activities of the whole right side of the heart. In Fig. 219 the pressure changes in the atrium, ventricle and aorta during one heart beat are schematically represented.

(1) *Physiological Venous Pulse (Normal Phlebogram)*

The tracing of the physiological venous pulse (Fig. 220) presents ordinarily three positive waves, designated respectively, *a, c* and *v*. Of

Fig. 220.—Simultaneous Tracings of the Carotid and Venous Pulses, etc. (From W. H. Howell, "Textbook of Physiology," published by W. B. Saunders Co.)

these, the *a*- and *v*-waves are the more constant, the *c*-wave sometimes being almost, or wholly, imperceptible. The two main depressions on the wave are designated by the letters *x* and *y*.

The *a*-wave, usually the highest elevation, is simultaneous with atrial systole, and due to it; it is therefore known as the *atrial wave* (or *auricular wave*).

The *c*-wave is approximately synchronous with the main wave of the carotid pulse. For a time it was supposed to be due to a transmitted impulse from the artery and was therefore called the *carotid* wave. It has been definitely shown, however, to be due to the transmission, to the blood in the right atrium and the jugular vein, of the shock imparted to the atrioventricular septum by the contraction of the right ventricle. The flow of blood from the coronary veins into the atrium occurs also at this moment and may be a contributing factor. The wave may still be designated the *c*-wave, though it is independent of the carotid pulse.

Regarding the origin of the *v*-wave, there has been considerable difference of opinion, some authors believing it to be due to stagnation of blood with gradual rise of pressure in the atrium, subsequent to closure of the tricuspid valves, during ventricular systole (ventricular-stasis theory of Hering), others looking upon it as a wave, occurring during the diastole

of the ventricle, due to a dislocation upward of the base of the heart at the moment when the systole of the ventricle ceases and its diastole begins. Both factors, in all probability, play a part. In the majority of instances, the crest of the *v*-wave is protodiastolic in time, though the earlier portion of the ascent is telesystolic in time; an encroachment of the crest of this wave upon systole indicates an impending (or already existing) tricuspid insufficiency.

The main depression, *x*, corresponds to the collapse of the vein that occurs immediately after the atrial systole at the beginning of atrial diastole. Since this moment coincides with the early part of ventricular systole, the veins on inspection are seen to undergo a systolic collapse. For this reason, the physiological venous pulse is often spoken of as a *negative venous pulse;* but since the positive waves on the physiological venous pulse are presystolic (*a*-wave) and diastolic (*v*-wave) in time, this pulse is also sometimes referred to as the *diastolic-presystolic venous pulse.* It is these two positive waves and the collapse of the vein after each of them that give rise to the "double venous pulse" seen on inspection in conditions of slight venous stasis and in some healthy persons during each cardiac revolution.

The lesser depression on the phlebogram, designated as *y*, lies between the *v*-wave and the *a*-wave; it is therefore a diastolic collapse, and is due to the flow of blood out of the right atrium into the ventricle just before the atrium contracts.

When the heart is beating slowly, additional waves may sometimes be seen upon the venous pulse, even in health. One of these wavelets, known as the *h*-wave (Hirschfelder), follows the *v*-wave by a definite interval and is believed to be due to the snapping together of the atrioventricular cusps at the end of ventricular filling in mid-diastole. It corresponds in time to (1) the third heart sound, (2) the onset of Henderson's period of diastasis, and (3) the minute *p*-wave sometimes seen on the cardiogram.

(2) *Abnormal Forms of Venous Pulse*

A whole series of abnormalities of the venous pulse have been described. To avoid confusion it is best to familiarize oneself first with two or three characteristic deviations from the normal and, later, as one's knowledge grows, to undertake the study of less common abnormalities. Only the common types will therefore be referred to here; namely: (1) the venous pulse of atrial paralysis (or atrial fibrillation); (2) the venous pulse of outspoken tricuspid insufficiency (typical ventricular venous pulse).

The Venous Pulse of Atrial Paralysis (or Atrial Fibrillation).—When the right atrium is paralyzed (or is shown by the electrocardiogram to be

fibrillating), the *a*-wave disappears from the venous pulse and only the *c*- and *v*-waves are recognizable. The *x*-depression becomes less marked. This form of phlebogram is most often met with when the arteriogram reveals a pulsus irregularis perpetuus. In the electrocardiogram, simultaneously recorded, the normal *P*-wave has disappeared; in its place one sometimes sees a number of small elevations due to the electrical variations that accompany atrial fibrillation (*q. v.*).

Fig. 221.—Phlebogram from a Patient Suffering from Paralysis of the Right Atrium. Drum Moving Rapidly. Disappearance of *a*-wave. Arteriogram for Comparison. (Personal Observation, J. H. H. Bull.)

Venous Pulse of Outspoken Tricuspid Insufficiency (*Ventricular Venous Pulse*).—In marked tricuspid insufficiency, all three positive waves of the normal venous pulse disappear and each systole of the heart is accompanied by a single huge broad wave on the venous pulse. This single large wave is due to the direct propulsion of blood by the contracting right ventricle into the right atrium and jugular vein through the insufficient tricuspid valve. This is the typical *ventricular type* of venous pulse. Since the dilatation of the vein is synchronous with ventricular systole, this pulse is often spoken of as a *positive venous pulse*, in contrast with the negative venous pulse (or systolic collapse) seen under normal conditions. This type of venous pulse, when outspoken, is easily recognizable by the naked eye, since (1) it is single instead of double, and (2) the positive wave is systolic in time (synchronous with the apex beat and carotid pulse). Occasionally, before the atrium is paralyzed, the ventricular wave is preceded by an *a*-wave.

Fig. 222.—Phlebogram in a Case of Tricuspid Insufficiency with Cardiogram for Comparison. (Personal Observation, J. H. H. Bull.)

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F. Electrocardiograms

Our chief object in graphic registration is to determine the actual sequence of events in the cardiac cycle. It is obvious that the fewer sources of error there are in the method, the more accurate will be our knowledge of the heart's action. In phlebograms, cardiograms, and arteriograms, we record the heart's action only indirectly in the form of secondary changes produced in the blood stream. These, in turn, we must mentally transpose to those phases of the contraction of the heart that probably produce the different waves in the vessels. These pulsations are easily subject to modification from causes entirely outside of the heart, such as engorgement of, or pressure upon, the vessels, or even by the method used to record the pulsation.

We have, however, a method that seems to eliminate most of these difficulties, and that gives us an accurate means by which we can determine the actual form of the cardiac contraction. This is electrocardiography, a description of which has already been given. The cardiac electrical variations that are recorded by this method have been shown to be the same whether they are led off from the heart itself, or from distant parts of the body. Therefore, secondary modifications do not have to be considered in interpreting the waves obtained in their relations to the various phases of the heart's action.

These electrical currents are given off from the muscle at a time about 1/100 of a second prior to the actual mechanical contraction. They are products of the stage of readjustment within the muscle between the times of stimulation and contraction, or what is known as the period of excitability. Since, however, contraction always follows the course of excitation, for all diagnostic purposes this time relation can be disregarded and the electrical waves are often referred to as indicating the path of "contraction."

The curve obtained by electrocardiography (see p. 783) is known as an **electrocardiogram.** The summation of action currents in the heart muscle thus recorded gives us clews to the origin and course of excitations in the heart muscle, and thus, indirectly, also, as to the course of the contraction wave as it passes over the heart.

1. The Electrocardiogram of a Normal Heart

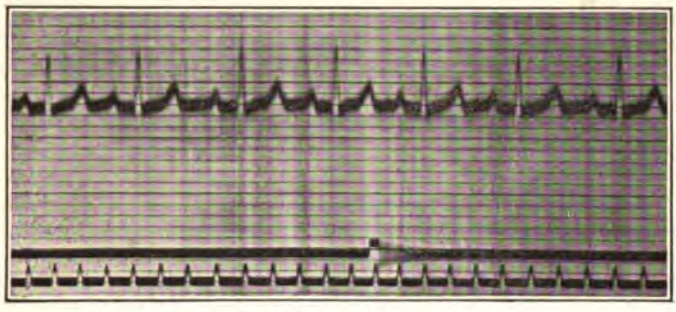
For the excitations belonging to one cardiac cycle, we find in an electrocardiogram of a normal heart—known as a normal or typical EK—a rather complicated curve. First, there is a small upward wave, *P.* This is followed by a pause, after which we see a small downward wave, *Q,* then a high upward wave, *R,* followed by a second downward wave, *S,* then a medium-sized upward wave, *T,* and, finally, a pause at the end of the cycle, which ends with the appearance of the next cardiac cycle.[1]

In all three leads (or derivations), the three main waves

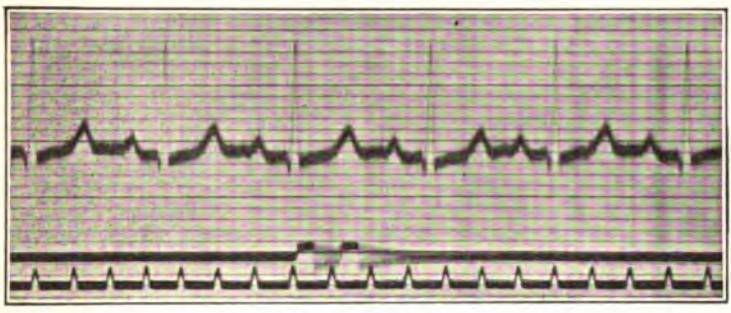
[1] Often, after the *T*-wave there is still another small upward wave, the *U*-wave (see Lewis and Gilder).

are visible, though the height of the waves may vary somewhat for the different leads.

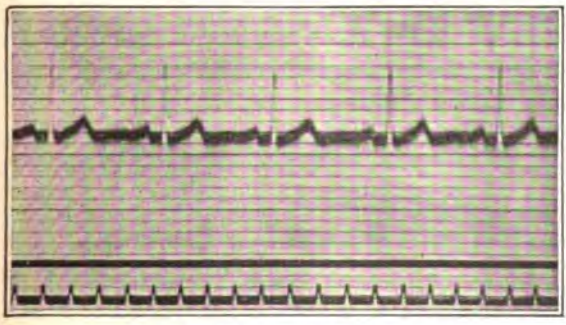
The *R*-wave is always the largest wave, and normally the *T*-wave is

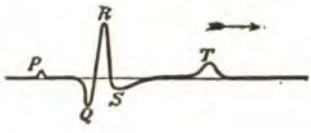


I. Right Arm and Left Arm.



II. Right Arm and Left Leg.





III. Left Arm and Left Leg.

Fig. 223.—Normal Electrocardiograms Obtained by Photographing the Movements of a Sensitive Galvanometer. Waves with the Apex Upward Indicate that the Base of the Heart (or the Right Ventricle) is Negative to the Apex (or Left Ventricle). Waves with the Apex Downward have the Opposite Significance. Wave *P* is Due to the Contraction of the Auricle. Waves *Q*, *R*, *S*, and *T* Occur During the Systole of the Ventricle. The Curve Seems to Show that the Contraction in the Ventricles Begins First Toward the Apex (or in the Left Ventricle), Since the Negativity First Appears Toward that Side (Wave *Q*).

taller and broader than the *P*-wave. The *P*-wave corresponds to the excitation of the atria; the *Q, R, S, T* complex corresponds to the excitation of the ventricles.[1]

It is believed by Einthoven that the *P-R* interval corresponds to the period of conduction of the excitation from the atria to the ventricles along the atrio-ventricular bundle of His. Arriving in the Purkinje system, the excitation reaches a large number of spots in the walls of the ventricles almost simultaneously. Should the excitation of the ventricle occur first near the heart's apex, there is a well-marked *Q*-depression, but should some other portion of the ventricle be first excited the *Q*-depression does not appear. The *R*-wave is evidence of the predominance of the excitations, at the moment, in the wall of the right ventricle and at the base of the heart, while the subsequent *S*-depression points to a temporary predominance of excitation in the left ventricle and in the apical region. The interval between (*Q, R, S*) and *T* and the *T*-wave itself correspond to a period in which the whole musculature of both ventricles is excited. Should the excitation cease in the left ventricle before it does in the right, the *T*-wave becomes negative instead of positive; should the base of the heart remain excited longer than the apex, the *T*-wave in Lead III is directed upward, while if the apex remains longer excited than the base, the *T*-wave in Lead III is directed downward. According to Kraus and Nicolai, the *R*-wave depends upon excitation of the papillary muscles, the *R-T* interval corresponds to the period of excitation of the main muscle-bundles of the ventricles, and the *T*-wave is due to excitation at the base of the heart.

Other observers deny a relationship of the form of the EK to the complicated course followed by the excitation through the heart muscle. Thus Frédéricq believes that the form is due to a peculiarity of the heart muscle and that it may be obtained by registering the currents from an isolated strip of heart muscle; his view is not unlike that of Eyster, who got *R*- and *T*-waves from isolated strips of terrapin ventricle. Straub and Hoffmann suggest that the EK is not the result of the excitation process alone but depends also upon the contraction process and upon metabolic changes.

Florence Buchanan believes that the *R*-wave is due to a slight asynchronism between the two ventricles.

As a matter of fact, the real explanation of the waves of the ventricular complex must still be awaited.

One must always bear in mind that the heart's contraction is not a single muscular action, but a coördinate movement of many parts, and the electrical

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[1] Nicolai has introduced another terminology, in which he has attempted to signify the cause of each wave by the letter applied to it. The first or atrial wave he calls *A* (= *P*-wave of Einthoven). The ventricular contraction being represented by two main waves, the first is lettered *I* for initial contraction (= *R*-wave of Einthoven) and the second *F* for final contraction (= *T*-wave). Depressions below the base line are lettered *a* and *p* according to their relation to the three main waves. For example, the *Q*- and *S*-waves are in this nomenclature called *Ia* and *Ip*. The space between *A* and *I* is termed "*h*," as it represents the time taken for the stimulus to pass over the bridge. That between *I* and *F* is termed "*t*," for during this time the ventricular muscle or "Triebwerk" contracts. That between *F* and *A* is known as "*s*," as it represents the diastolic pause. Most writers have adhered to the terminology of Einthoven.

curve obtained is the resultant of a large number of component electrical potentials. Any change in the position or relative strength of contraction of any portion of the heart will disturb this equilibrium and modify the form of the electrocardiogram. This is particularly striking in the interaction of the musculature to the right and left of the heart's axis. Waller has applied to this the principle and arithmetical formula of the mechanical balance, and calculates, from the electrocardiographic curves, the angle of inclination of the heart's axis in relation to the midline of the thorax.

It seems fairly certain, however, that the action currents begin during excitation of a part and before its actual contraction. According to Einthoven, the first electrical deviation in the ventricular complex of the EK occurs about 0.03 sec. before the first sound of the heart occurs as shown by mechanical registration, and about 0.06 sec. before the main oscillations of the first sound occur. Again, the EK precedes the contraction of the anterior wall of the ventricle by 0.03 sec., and the *R*-wave has been finished for 0.65 sec. before there is a rise in the intraventricular pressure. The end of the *T*-wave coincides approximately with the end of the expulsion-time of the ventricle.

2. Clinical Value of Electrocardiography

Electrocardiography has not only made us acquainted with a whole series of new facts regarding the origin and conduction of excitations within the heart, but it has greatly simplified the diagnosis of the several forms of cardiac arhythmia. While these arhythmias could, it is true, be analyzed before the advent of electrocardiography by means of the arteriograms and phlebograms obtained by sphymography, still the securing of electrocardiograms and their analysis are relatively simple compared with the difficulties, the tedium, and the circumstantiality of securing the sphygmographic data. As a matter of fact, when a heart station, equipped with a modern electrocardiograph, is available, sphygmography can, for the majority of clinical purposes, be entirely dispensed with. The information desired can be more quickly, more easily, and more certainly gained by electrocardiography. Indeed, if we except the usefulness of venous pulse-tracings for the diagnosis of tricuspid insufficiency and of pulsus alternans, electrocardiography has relegated sphygmography to a place of scarcely more than historical interest.

3. Physiological Variations of the Electrocardiogram

***P*-Wave.**—Usually a single wave, it may be double, even normally, especially in Lead III. In dextrocardia, the *P*-wave is negative. But a normally situated and functioning heart may occasionally yield a negative *P*-wave in any one or in all three of the leads.

***Q*-Wave.**—This is not always present, or if present, may be very indistinct. Not infrequently, it is better marked in Lead III than in Leads I and II.

***R*-Wave.**—Always the highest wave, it is, however, subject to great variations in height. It is smaller in Lead III than in Leads I and II. In hypertrophied hearts, the *R*-wave may be very high.

***S*-Wave.**—This is usually best marked in Lead III, and most indistinct in Lead I. It seems to be exaggerated when the heart tends to be more horizontally placed in the thorax than normal. It was, formerly, believed to be especially pronounced in neurasthenic states and was even dubbed the "neurasthenic wave," but this idea no longer prevails.

***T*-Wave.**—This wave is extraordinarily variable, not only in height but also in breadth. Usually positive, it is sometimes negative normally, and may even be diphasic. As age advances, the *T*-wave becomes less pronounced (Nicolai). By some it is thought that a flattening of the *T*-wave is an early sign of myocardial insufficiency, but this view is strongly combated by others.

***P-Q* Interval.**—This interval, now called the **"alpha interval,"** averages 0.1 sec. in normal duration. In tachycardia, it is much briefer. In cases of delayed conduction, this interval may be greatly lengthened. Thus Hoffmann describes cases in which the interval was 0.23 sec., and my colleague, Prof. W. S. Thayer, has studied a pathological case in which the alpha interval had the astonishing length of 0.6 sec. In one of my own patients, now under observation, the conduction time is lengthened for some beats; in an EK made for me by Dr. Bridgman the *P-R* interval was, for a single cycle, no less than 1.03 second! The duration varied considerably in other cycles.

***S-T* Interval.**—This interval, now called the **"beta interval,"** may also vary considerably under normal conditions, depending mainly upon the rate of the heart. It is usually horizontal in course above the abscissa, but it may rest upon the base line and is sometimes slightly curved.

***T-P* Interval.**—This interval, now called the **"gamma interval,"** also varies in length. In it, as was mentioned above, we sometimes meet with a *U*-wave. Thus, in one report, a *U*-wave was present in 44 out of 49 persons in Lead II.

Age Differences.—The EK, in childhood, has been studied especially by Nicolai and Funaro; in old age, by A. Hoffmann and by Nicolai. In sucklings, the *S*-wave is large and the *T*-wave small. In the senile heart, the *R*-wave may be negative in Lead III and the *T*-wave [illegible] same lead.

According to Nicolai, the general rules hold: (1) tha the *R*-wave gets larger and the *T*-wave smaller; (2) th blood pressure the *R*-wave gets larger and the *T*-wave later smaller; and (3) that as the heart increases in si comes larger and the *T*-wave gradually smaller.

4. The Electrocardiogram in Pathological States

It must be emphasized at the beginning that one must not expect the EK to yield information that it is incapable of giving. Above all, it should be recognized that the EK is not a measure of the functional capacity of the heart in the ordinary sense of that term. For a man with outspoken myocardial insufficiency (dyspepsia, cyanosis, anasarca, dilated heart), may still have an electrocardiogram exhibiting waves indistinguishable from those obtained from a normal person. Moreover, when compensation is reëstablished by rest, diet and strophanthin, the curve may be the same as in the stage of decompensation.

Certain conclusions regarding (1) the size of the heart chambers, (2) the position of the heart, and (3) above all, the disturbances of rhythm of the heart, can, however, be drawn from the EK.

Size of the Heart Chambers.—A careful study of the height of the waves in different valvular lesions has been made by Steriopulo. The results are shown in the following table in which the highest *R*-wave (in aortic insufficiency) was taken as 100 and the height of the other waves were compared with it:

Wave	Mitral Stenosis	Mitral Insufficiency	Aortic Insufficiency
P	20.6	9	12
R	34.6	42	100
T	21.3	16	10

The high *P*-wave in mitral stenosis is a striking feature, due probably to atrial hypertrophy. The very high *R*-wave in aortic insufficiency may depend upon the hypertrophy of the left ventricle. The marked *S*-wave in mitral insufficiency is also interesting.

Position of the Heart.—In *true dextrocardia*, in which the heart is on the right side with its long axis extending from the left above to the right and downward, we get a mirror picture of the normal electrocardiogram, in that the waves *P*, *R* and *T* are all directed downward. In *false dextrocardia*, in which the heart is merely displaced to the right by a pleural effusion or by retraction of the thorax, this reversal of the curves does not occur. In *congenital heart disease*, the *P*- and *T*-waves are positive while the *R*-wave is negative.

Disturbances of Cardiac Rhythm.—Here the EK gives us information of the greatest clinical value. To-day, in the heart station of our larger clinics, an EK is made as a routine measure in patients exhibiting

tachycardia, bradycardia, respiratory arhythmia, extrasystolic arhythmia, perpetual arhythmia, or conduction disturbances causing partial or complete heart block.

The electrocardiographic findings in these various states are described further on. (See Clinical Disorders of the Heart Beat.)

5. The Electrocardiogram in Experimental Physiology

One great advantage derivable from electrocardiography is the possibility of subjecting ideas, arrived at by the clinical study of patients suffering from cardiac disease, to experimental test. If, for example, a patient yields an atypical EK and we think this might be accounted for by a given lesion in the heart, or by the origin of an excitation at some abnormal site, we may go into the laboratory and produce this hypothetical lesion in an animal or stimulate the animal's heart at the unusual site postulated, and make an EK to see if it agrees in form with the one obtained from the patient.

This imitation of clinical disorders by laboratory experiment is proving to be exceptionally useful in the study of disturbances of the heart beat. Our conceptions of cardiac disease are being rapidly altered by the thorough application of graphic and of experimental methods. If one compare the chapter on diseases of the circulation in an up-to-date text with the chapter on the same subject in a text of ten years ago, he will easily confirm his conviction regarding the evolution of ideas that has been taking place. In America, Cohn, James, Williams, Hirschfelder, Bond, Bridgman, Eyster, Meakins, the Oppenheimers, White, Carter, Rothschild and others have been engaged in this work. In England, aside from the pioneer work of Waller, Bayliss and Starling, brilliant experimental work has been carried on by Thomas Lewis and his associates in London, and by Gotch and Florence Buchanan at Oxford. Those interested should read the "Lectures on the Heart" recently delivered in this country by T. Lewis.

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G. Measurements of Blood Pressure

(Sphygmomanometry, or Tonometry, of the Blood Vessels)

1. Introduction

Methods of determining, clinically, the maximal (systolic) and minimal (diastolic) pressure in the arterial system, and of measuring the pressure in the superficial veins, have been worked out and are of value for diagnosis. By blood pressure is meant the pressure exerted by the blood at any selected point in the circulation at a given moment, either on the blood current lying in front of it (end pressure) or on the vessel wall (lateral pressure). The pressure on the wall of the vessel is a little less than that on the column of blood in front, since the latter includes not only the pressure proper but also the force in the stream itself. The pressure varies at different points (intraventricular, aortic, brachial, radial, capillary, venous, intra-atrial). Clinically, we measure the arterial pressure in the brachial artery and the venous pressure in the veins of the hand the median vein at the elbow.

In physiological experiments, *cannulae* can be introduced into o sels for measuring the blood pressure, but in clinical work we us methods of determination.

Definitions.—By MAXIMAL ARTERIAL BLOOD PRESSURE PRESSURE is meant the highest point reached by the blood pr

artery during the ventricular systole (pulsatory blood pressure maximum). By MINIMAL ARTERIAL BLOOD PRESSURE OR DIASTOLIC PRESSURE is meant the lowest point reached by the blood pressure within the artery during ventricular diastole (pulsatory blood-pressure minimum).

If we subtract the minimal from the maximal blood pressure, we obtain what is known as the PULSE PRESSURE or *pulse-pressure amplitude*. For example, if the systolic pressure be 124 and the diastolic pressure 84, the pulse pressure is 40. The term MEAN PRESSURE is used to designate the average pressure *during a certain period*, not the arithmetic mean between the maximal and minimal pressures.

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2. Instruments for Determination of Ar Pressure

The earlier instruments employed for clinical use we momanometer of von Basch, (2) that of Riva Rocci, an ter of Gärtner. There are now a number of modificatio ments and it is unnecessary to describe all of them.

The principles underlying all these instruments for bloodless blood-pressure determinations are the same: (1) the arterial pulse is obliterated by compression from without by means of a cuff; and (2) the pressure necessary for this is measured by some form of manometer. By the older methods, only the systolic pressure could be measured; the newer instruments permit of accurate determinations of both systolic and diastolic pressure.

(*a*) *The Cuff for Compressing the Arm*

The arm is encircled by an elastic cuff or arm band, which, when inflated by pumping air into it, obliterates the arterial pulse below the cuff as soon as the pressure within has been sufficiently raised. It is best quickly to increase the pressure to some point above that necessary to obliterate the radial artery, and then to allow the air smoothly to escape until the pulse just reappears in the radial artery. This point corresponds to the maximal systolic pressure; that is, an external pressure has been supplied just sufficient in amount to overcome the internal resistance, which includes, in addition to the blood pressure, the force of the stream, the arterial wall, and the surrounding soft tissues. Comparative observations on animals show that readings thus obtained differ by only a few millimeters from direct blood-pressure readings obtained by the insertion of a cannula into the artery.

The width of the cuff is very important. In the original Riva-Rocci instrument the cuff used was only 5 to 6 cm. broad and the readings obtained were 40 per cent too high, owing to the fact that a part of the pressure in the cuff was used up in dislocating the soft parts of the arm. The error was especially great in stout people. If, as suggested by v. Recklinghausen, a cuff 12 to 15 cm. broad be used, the error is much smaller, amounting to only about 10 per cent, as has been proven by experiments on human beings in which a cannula has actually been inserted into the open artery for control (amputations).

In children, a cuff 7 cm. in width is sufficient.

It is customary to apply the cuff over the upper arm, a little above the elbow. The sleeve of a thin shirt, or of a thin blouse, between the arm and the cuff is not objectionable. The error when the cuff is thus applied is less than when a tight sleeve is rolled up above a cuff in order to apply the latter directly to the skin. The reasons for choosing the brachial artery in blood-pressure determinations are, according to Janeway, as follows: "It gives us the systolic lateral pressure within the subclavian, since brachial and axillary are continuous in direction, and therefore a near approximation to systolic lateral pressure in the aorta. This, combined with estimation of diastolic lateral pressure in the brachial, which is practically the same as aortic diastolic pressure, gives the best insight into actual variations of systemic blood-pressure." It must be remem-

bered, however, that though the brachial pressure is generally equal to that in the aorta, it is not always so. There are observations that indicate that the pressure in the brachial arteries of the two sides may, in the same person, vary as much as 20 mm. (Bing).

(*b*) *Manometers for Measuring the Pressure Within the Cuff*

Several varieties of manometer are in use. They include (1) mercury manometers, (2) compressed-air manometers, (3) aneroid manometers, and (4) spring manometers.

Mercury Manometers.—Two main types of these have been introduced: (1) the *reservoir type,* and (2) the *U-shaped type.*

Reservoir Type of Mercury Manometer.—The *Riva Rocci* is the typical example of the reservoir type.

The Riva-Rocci Instrument.—Many modifications of the Riva-Rocci instrument are on the market, including (1) the *new Nicholson* (probably the best), (2) the *Cook,* (3) the *Staunton,* and (4) the *Hill* instrument. Other similar instruments are the Kercher, the Gärtner and the Westenrijk.

Fig. 224.—The New Nicholson Sphygmomanometer. When Closed, the Instrument Fits into a Morocco Pocket-case, which Contains also the Bulb and Cuff. (By courtesy of Precision Ther. and Inst. Co., Philadelphia.)

The new Nicholson-Princo sphygmomanometer comes in a neat case and is easily portable. It yields reliable readings, and has a stopcock that can be closed if one wishes to maintain the pressure for any length of time.

U-Shaped Mercury Manometers.—The two best instruments of this type are (1) *Janeway's sphygmomanometer,* and (2) *Faught's mercury sphygmomanometer.* Other instruments of similar type are those introduced by Martin, by Linnell, by Mercer, and by Fellner.

The *Janeway instrument* is very popular among American physicians. The manufacturers now supply it with a little metal-valve pump instead of the rubber bulb formerly used.

Another instrument, popular in this country, is that of *Faught.* It is compact, makes use of a metal pump, and of a special expansion tubing for the inflator.

Compressed-Air Manometer
nometers of this type are also
ient. A little colored liquid, or
mercury, is placed in the bulb
a glass tube. On raising the
drop of this fluid is force
tube and is an index

the height of the pressure can be read. The *Oliver mercurial compressed-air manometer* is perhaps the best known instrument of this type.

Bendick's air-water sphygmomanometer and Hertz's sphygmomanometer are other examples.

Aneroid Manometers.—These are very convenient for bedside use, being small and easily portable. They may require, however, to be adjusted, at intervals, on comparison with a mercury manometer. Many physicians prefer a mercury manometer for office work and use an aneroid manometer for house-to-house visits. Of the several aneroids on the market, the best known are (1) the *Rogers-Tycos,* (2) the *Faught aneroid,* and (3) *Pachon's sphygmometric oscillometer.*

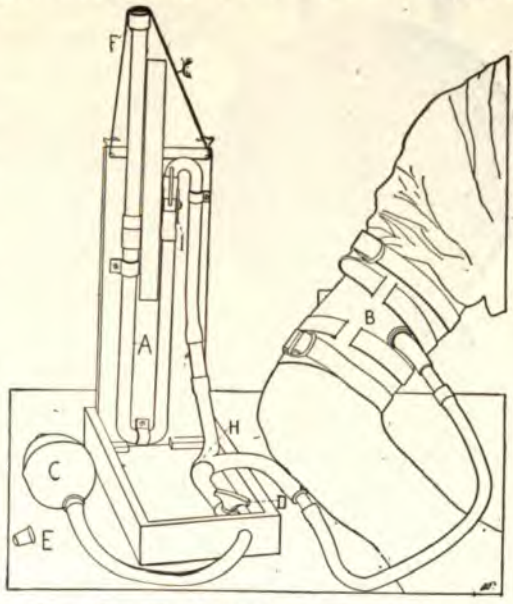

Fig. 225.—The Janeway Sphygmomanometer.
(By courtesy of Dressler-Beard Mfg Co.)

I have myself used the Rogers-Tycos instrument for a number of years

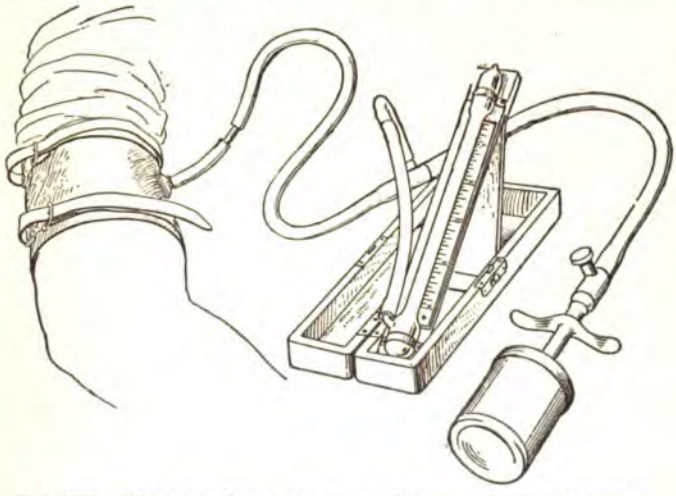

Fig. 226.—The New Oliver (Compressed Air) Sphygmomanometer.
(By courtesy of Dressler-Beard Mfg. Co.)

with satisfaction. Bachman praises highly Pachon's instrument. It is said, however, that the latter yields systolic readings 20 to 40 mm. Hg.

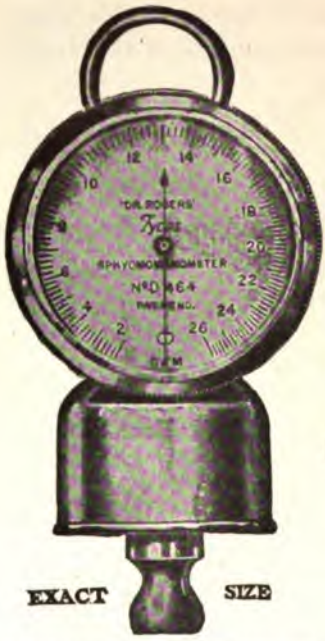

Fig. 227.—Tycos Sphygmomanometer. Method of Use: Pointer on Dial Operated by an Aneroid Chamber of Corrugated Metal—Not a Spring. (By courtesy of Taylor Instrument Co., Rochester, N. Y.)

higher than does the Staunton appa
though its diastolic readings show les
crepancy.

Other types of aneroid manomete
the market are (1) Brunton's, and (2)
quet's.

Spring Manometers. — An instr
much in use in Germany is *von Rec
hausen's tonometer.* I have used th
strument and find it very clumsy. It
less satisfactory than the instrume
general use in this country.

(c) *Instruments for Graphic Regist
of Blood Pressure*

For the most careful studies, g
tracings of the radial pulse may be
while the pressure in the cuff is fallin
a level above that of the systolic press
a level below that of the diastolic
sure. For ordinary clinical purpose
is entirely unnecessary, but when or
research is being carried out, it m
desirable to employ this method. O
instruments in use for this purpos
most convenient is *Erlanger's sph
manometer.* Other instruments much
in this way are A. G. Gibson's re
ing sphygmomanometer, C. Singer's in
ment, Uskoff's sphygmotonograph, Si

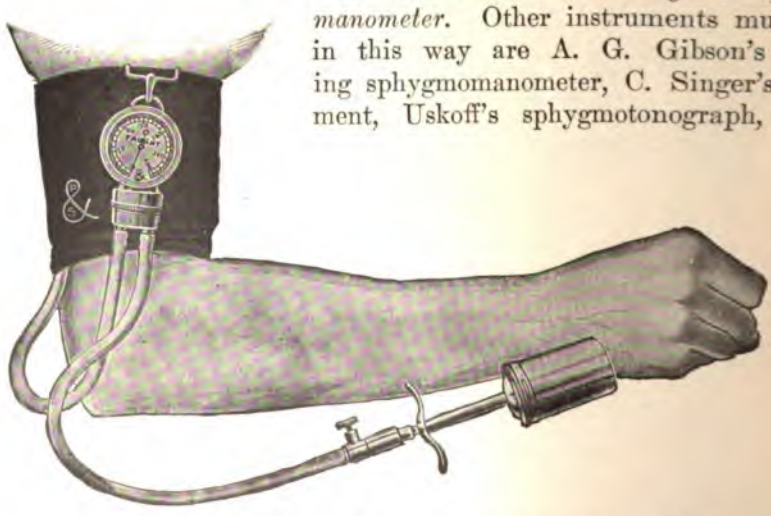

Fig. 228.—Faught's Blood-pressure Apparatus. Aneroid Type. (By courtesy of G. P. Pilling & Son, Philadelphia.)

mann's tonograph, Muenzer's sphygmoturgograph, Brugsch's sphygmotonograph, Fleischer's turgograph, and Bussenius' sphygmotonograph.

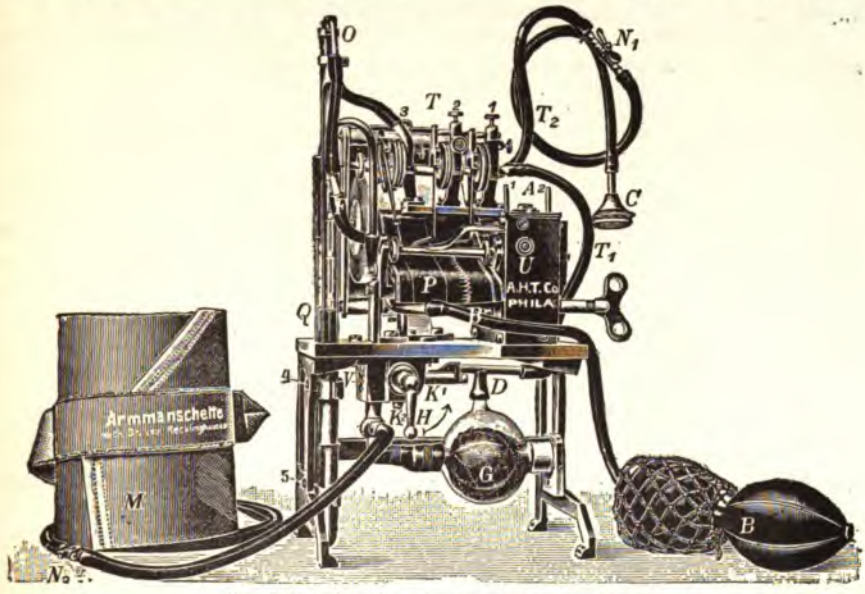

Fig. 229.—Uskoff's Blood-pressure Apparatus.
(By courtesy of A. H. Thomas Co., Philadelphia.)

(*d*) *Oscillatory Instruments*

In addition to those already described, mention should be made of certain instruments fitted with oscillating devices, intended to magnify (indirectly) the fluctuations of the mercurial column or of the pulsations in the cuff. They have been especially useful in the study of diastolic pressure. Among these may be mentioned, Bing's sphygmomanometer, Pal's sphygmoscope, Feddé's oscillometer, Widmer's oscillomanometer, and Vaquez's sphygmosignal.

(*e*) *Selection of an Instrument for Measuring Blood Pressure*

For ordinary clinical work, I would advise either a small aneroid manometer (Rogers-Tycos or Faught) or a simple mercury manometer of the Riva-Rocci type (new Nicholson, Janeway or Faught). I advise using the palpatory method for the determination of the systolic pressure, and the auscultatory method for the determination of the diastolic pressure.

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3. Determination of the Maximal (Systolic) Arterial Pressure

(*a*) *The Palpatory Method*

This is probably the best method for clinical determinations of maximal pressure. The cuff, 12 cm. in width, is applied on the arm and inflated until the radial pulse disappears. Air is then allowed cautiously to escape until the radial pulse suddenly reappears. The exact moment is easy to determine. On watching for the return of the radial pulse the artery should be palpated with the ball, rather than with the tip, of the finger.

The patient should be examined in the sitting or rec
A first reading may be quickly made to prove to the pati
cedure is harmless and not painful. This reading may be
subsequent reading accurately made. If the patient be ex
this should be noted and a later reading made. The arm
compressed long and the pressure should be allowed to

observations, sufficient time between readings being permitted for the venous pressure to fall to the normal level.

Sometimes, a few beats will go through to the wrist at a much higher pressure than the majority of beats; if so, this fact should be noted.

(*b*) *Oscillatory and Auscultatory Methods*

These methods can be used also for the determination of the maximal systolic pressure, but are less satisfactory than the palpatory method above described. For the details of these methods, the reader may consult the treatise of Norris or that of Janeway.

4. Determination of the Minimal (Diastolic) Arterial Pressure

One may use the palpatory, the oscillatory or the auscultatory method. For very exact determinations by the oscillatory method, the Erlanger instrument is perhaps best; but for all ordinary clinical work, the auscultatory method of Korotkow is strongly recommended.

(*a*) *Palpatory Method* (*Janeway*)

By this method the amount of external pressure, just sufficient to make the pulse, peripheral to the site of compression, begin to become smaller, is regarded as the "palpatory minimal arterial pressure." If, for example, the maximal blood pressure in the brachial artery amounts to 115 mm. of mercury and the minimal pressure to 65 mm., the pressure in the radial artery will vary by about 50 mm. with every pulse beat. If one now blow up the cuff on the arm so that the manometer indicates a pressure of 70 mm., the artery is closed until, with the rise of the pulse wave, the internal pressure reaches 70 mm.; a little less blood will therefore pass through and the pulse must become smaller. This diminution of the pulse can be felt on palpation, though it is best registered as a radial sphygmographic curve; while the pressure in the cuff over the brachial is gradually increased, every five millimeters of pressure-increase is noted on the radial arteriogram. Jacquet's sphygmotonograph or Uskow's instrument will be found convenient, permitting the recording of blood pressure in millimeters of mercury simultaneously and on the same strip with other tracings. The method yields results that are 25 to 30 per cent higher than the figures obtained when the open artery is used for control (Müller and Blauel). The palpatory method has given place to the auscultatory method.

(*b*) *Oscillatory Method* (*von Recklinghausen; Erlanger*)

If one observe the slightly oscillating level of the mercury meniscus in the manometer, or the very small excursions of the needle of a spring tonometer or of an oscillometer, when a pressure somewhat below the minimal pressure is determined by method (a), he will note that when the pressure is gradually increased a point will be reached where larger excursions suddenly appear. The pressure then existing is called the "oscillatory minimal arterial pressure" (Erlanger). As long as the pressure inside the artery is not compensated for by an equal external pressure, the arterial wall makes only slight excursions, but as soon as the external compression corresponds to the inner pressure, the arterial wall can float freely and will communicate large excursions to the air in the cuff. As soon then as the pressure in the cuff has just exceeded the minimal

Fig. 230.—Determination of Maximal and Minimal Pressure by Erlanger's Apparatus; Maximal Pressure at About 145, Minimal at About 95; Brachial Arteriogram Beneath. (Personal Observation, J. H. H.)

Fig. 231.—The Auscultatory Method of Determining Minimal Blood Pressure. (From G. W. Norris, "Blood Pressure: Its Clinical Applications," published by Lea & Febiger, Philadelphia.)

blood pressure (for a part of the pulse wave), the oscillations of the mercury or of the tonometer needle become larger.

(*c*) *Auscultatory Method* (*Korotkow*)

This is the simplest and, in my opinion, the best clinical method for determining the minimal pressure. It has been carefully controlled in my wards and can be warmly recommended.

A cuff is applied over the brachial artery and the pressure in it raised until the radial pulse disappears. The bell of the stethoscope is then placed over the ulnar artery close to the cuff. If the pressure in the cuff be now allowed to sink gradually one will hear a slight tone, usually at the moment the first pulse wave is felt at the wrist or a little earlier (maximal auscultatory arterial pressure). As the pressure is allowed to sink further, the tones accompanying the pulse beats grow louder and are sometimes accompanied by blowing murmurs. Soon after these become maximal, a point is reached when, on further lowering of the pressure, the sounds *suddenly become feebler* and soon vanish entirely. The sudden enfeeblement of the sounds corresponds exactly to the junction of larger and smaller oscillations in the preceding method and indicates the level of the "auscultatory minimal blood pressure." It is customary now to speak of FIVE DISTINCT PHASES as the sound varies during the fall of the pressure in the cuff.

First Phase.—When the pressure falls to the level of the maximal systolic pressure, an arterial tone is heard, not unlike the first sound of the

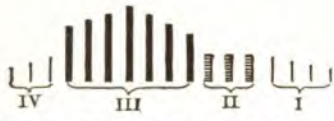

Fig. 232.—Gallavardin's Diagrammatic Representation of the Auscultatory Phases. I, Arterial Tone (Muffled); II, Tone and Murmur; III, Arterial Tone (Loud and Unaccompanied by Murmur; IV, Sudden Diminution and Muffling of Sound. The Beginning of IV Indicates the Diastolic Minimal Pressure. (From G. W. Norris, "Blood-Pressure: Its Clinical Applications," published by Lea & Febiger, Philadelphia.)

heart. It is due to the return of the pulse wave in the artery, the vibrations being supplemented by the resonance of the air within the cuff.

Second Phase.—As the pressure in the cuff falls further, the sound of the first phase is accompanied by a hissing murmur, due to the formation of a "liquid vein" as the blood flows through the constriction into the under artery below.

Third Phase.—As the minimal diastolic pressure is approached, the murmur of the second phase disappears, and a tone, usually much louder than that of the first phase becomes audible. The murmur disappears because the lessening of the constriction of the artery leads to a disappear-

ance of the "liquid vein." This third phase corresponds to the period of large oscillations in the curve obtainable by Erlanger's apparatus; it is the period of maximal arterial filling and collapse. The external pressure is now causing a partial flattening of the artery (MacWilliam & Melvin).

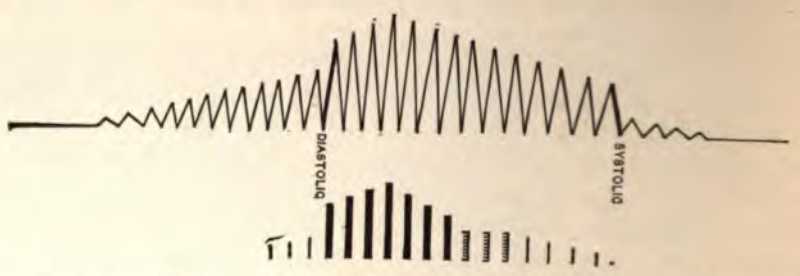

Fig. 233.—Gallavardin's Diagram Illustrating the Relationship Between the Oscillatory and the Auscultatory Phenomena. The End of the Third Auscultatory Phase Corresponds to the Last Large Oscillation. (From G. W. Norris, "Blood Pressure: Its Clinical Applications," published by Lea & Febiger, Philadelphia.)

Fourth Phase.—At the end of the third phase, if the sound be attentively listened to, it will be found to become diminished suddenly and markedly and to assume a muffled character (Ettinger, 1907). The *onset of this fourth phase indicates the exact moment in which the pressure within the cuff corresponds to the minimal (diastolic) pressure in the brachial artery.*

Fifth Phase.—The fourth phase is very short; at the end of it, the sound disappears entirely (fifth phase). These phases and their relations to the oscillations of the mercury column have been diagrammatically represented by Gallavardin. Careful studies of the duration of the different phases have been made by Goodman and Howell (1911).

For listening to the sounds in the radial artery on using the auscultatory method, Pilling's *bracelet stethoscope* is convenient. It may be used with any form of sphygmomanometer. After the arm band has been applied in the ordinary way above the elbow, the bracelet is adjusted over the radial artery just below the bifurcation. The sounds can then be observed very accurately.

The auscultatory method has one limitation; it is somewhat unsatisfactory when tones are audible in the peripheral arteries before the cuff is applied (*e. g.*, in aortic insufficiency); it can be used close attention to the beginning of the 4th phase; the

In recording minimal pressure in clinical historie mination (palpatory, oscillatory or auscultatory) sh tioned. While the auscultatory and oscillatory value accurately determined, the palpatory value is higher a somewhat different point on the blood pressure curve.

diastolic pressure within the artery is not quite identical with any of the clinically determined "minimal pressures"; the "maximal systolic pres-

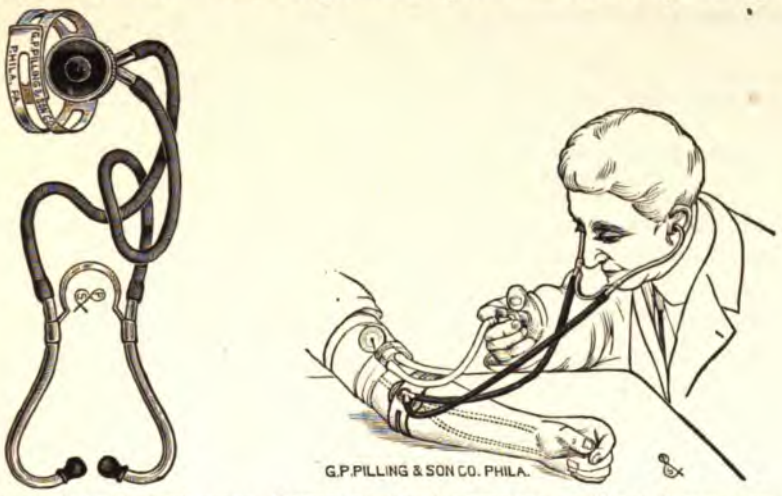

Fig. 234.—A Bracelet Stethoscope, Convenient for Observations on Blood Pressure by the Auscultatory Method. (By courtesy of G. P. Pilling & Son Co., Philadelphia.)

sure" as determined clinically undoubtedly approaches much more closely to the true systolic intra-arterial pressure.

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5. The Arterial Blood Pressure Under Normal Conditions

In young adults, between 20 and 25 years of age, the blood pressure, measured when the individual is reclining, averages 110 mm. maximal (systolic), 65 mm. minimal (diastolic), and 30-45 mm. pulse pressure (J. Erlanger).

In 1,000 presumably healthy individuals reported by Woley, the average maximal (systolic) blood pressure, determined with the Tycos instrument was as follows:—

Age 15 to 30	122
" 31 to 40	127
" 41 to 50	130
" 51 to 60	132

As the upper unit of normal, Woley regards 140 mm. at the period between 15 and 30, and 155 at 60. In women, the blood pressure normally averages 8-10 mm. below that of men of the same age.

In infancy, the maximal pressure is about 80 mm. (Trumpp). Up to the tenth year it rarely exceeds 90 mm.; at or near puberty it ranges between 90 and 110 mm.

(*a*) *Variations Under Physiological Conditions*

Gravity has a distinct effect as shown by *change in posture;* on standing, after lying recumbent, the minimal (diastolic) pressure rises, the pulse pressure decreases, and the heart rate is accelerated (Erlanger and Hooker).

The *eating of food* increases the maximal (systolic) pressure, the pulse pressure, and the heart rate.

The effect of *muscular exercise* is, at first, similar to that of eating, but on *fatigue* the blood pressure falls and the heart is slowed (Schott, Cabot).

It has been shown that *mental effort*, like stimulation of a sensory nerve, causes vasoconstriction, rise of blood pressure (especially of the minimal pressure), and acceleration of the heart rate. During *sleep*, there is a slight fall in maximal blood pressure and a marked fall in the minimal blood pressure.

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6. The Blood Pressure in Pathological States

(a) *Chronic Arterial Hypertension*

Among the pathological states in which the blood pressure may continue to be much higher than normal over a long period, may be mentioned: (1) increased intracranial tension, (2) chronic nephropathies, especially contracted kidneys, (3) aortic insufficiency, (4) certain forms of arteriosclerosis, (5) chronic polycythemia, (6) certain cases of Graves's disease, and (7) chronic cyanosis, especially that due to failing myocardium.

When there is an **increase of intracranial tension,** due to meningitis, brain tumor or other cause, the maximal blood pressure may become very high (300-400 mm. of Hg), the minimal blood pressure may rise to 160, and there is bradycardia. Whenever the intracranial pressure rises above the blood pressure, general vasoconstriction due to stimulation of the vasomotor center results; the blood pressure rises in a series of stages (Traube-Hering waves) until the mean blood pressure exceeds the intracranial pressure (Cushing). Nitrites do harm in such cases, though lumbar puncture or cerebral decompression may be beneficial by lowering intracranial pressure.

In **chronic diffuse renal diseases,** especially those in which the kidneys are contracted, high blood pressures (150 to 300 mm.) are common, though in some cases, not well understood as yet, the blood pressure may not be elevated. The cause of the arterial hypertension in chronic renal disease has been much discussed. Some have attributed it to narrowing of the renal arterioles and consequent defective elimination of urinary solids, especially of the non-coagulable nitrogenous substances of the blood. Experimental researches indicate that reduction of the amount of kidney substance in the body will lead to arterial hypertension and to hypertrophy of the heart. As endocrinology has advanced, theories that the hypertension is of hormonic origin have been advanced; thus some have held an internal secretion of the kidney (renin) responsible, others a hypersecretion of epinephrin (Vaquez, Neusser) with resulting epinephrinemia; neither theory has had, as yet, sufficient support.

According to Janeway, hypertension of renal origin may be due: (1) to a purely quantitative reduction of renal tissue with resulting hypertonus due to retained poisons, (2) to the poisons which intoxicate the nervous system giving rise to the symptoms which we call "uremic," (3) to a superimpositi
factor upon a hypertension due primarily to an irritability of the va
mechanism and which leads to general sclerosis of the small arteri
those of the kidneys.

Recently, Voegtlin and Macht have discovered a crystalline pres
not epinephrin, which stimulates the heart and causes pronounced vas
they believe it to be a derivative of cholesterin, and think that it
in the adrenal cortex. N. B. Foster, in 1915, reported the isolation o

substance from the blood of uremic patients, which may prove to be of great importance.

In nephropathic hypertension the maximal pressure is as a rule more increased than the minimal; there is, accordingly, a large pulse pressure. It has been shown that the minute-volume of the heart and the systolic output are normal or a little subnormal (Bergmann and Plesch) and the rate of flow is not increased (Stewart).

Apoplexy, uremia, myocardial insufficiency, paroxysmal dyspnea, Cheyne-Stokes breathing, and edema of the lungs are among the complications not infrequently encountered in cases of chronic hypertension.

In **aortic insufficiency**, the large pulse pressure depends upon (1) increase of maximal pressure (180-200 mm.) and (2) reflex decrease of minimal pressure (30-60 mm.). The main fall of pressure is systolic in time and is due to increased capillary flow, not to regurgitation into the heart in diastole (H. A. Stewart).

In aortic insufficiency, there may be a large difference (as much as 150 mm.) between the maximal blood pressure in the arm and that in the leg, when both are measured when the patient is in the recumbent posture. Under normal conditions, these pressures are equal.

Among the **forms of arteriosclerosis** accompanied by arterial hypertension, that in which the small arterioles are principally involved (arteriocapillary fibrosis, arteriolar sclerosis) is the most important. Even then, it may be the involvement of the renal arterioles that counts most. The larger arteries, like the brachial and radial, may be extensively sclerosed without causing hypertension.

The high blood pressure due to vasoconstriction before arteriosclerosis has set in is called *hyperpiesis* (Allbutt). Patients suffering from arteriosclerosis are more prone than normal individuals to suffer from *crises of vasoconstriction*—the so-called "vascular crises" (Collier; Pal). Such crises are common also in tabes, in lead poisoning, in pregnancy, and in the nephropathies. Here belong angina pectoris, angina abdominis, crises of constriction of the cerebral arteries, and intermittent claudication. In these vascular crises, the maximal pressure may rise 40-80 mm. of Hg. A patient with angina pectoris may have a low blood pressure ordinarily and high pressure during his attacks.

In one form of **chronic polycythemia**, sometimes designated "polycythemia hypertonica" (Geisbock), arterial hypertension is present. The cause of the hypertension is not known.

In **Graves's disease**, the blood pressure may be normal or low, but in some cases, outspoken arterial hypertension is present. When the blood pressure is high in exophthalmic goiter, the cause is to be sought, not in the thyreointoxication directly, but rather in the secondary processes in the heart, blood vessels or kidneys.

In **chronic cyanosis**, due to a failing heart, the arterial hypertension may be marked, due to overloading of the blood with CO_2 and stimulation of the vasoconstrictors as in experimental asphyxia. This form of high blood pressure associated with venous stasis has been carefully studied by Sahli, who calls it "high pressure stasis." Cardiotonic therapy will often reduce the blood pressure in these cases by overcoming the myocardial insufficiency so that the blood is better aerated.

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(*b*) *Acute and Chronic Arterial Hypotension*

A persistently low blood pressure is more often due to loss of arterial tonus than to failure of the heart. Hypotension is common in (1) acute infections, (2) pulmonary tuberculosis, (3) surgical shock, and (4) chronic wasting diseases of various sorts.

In **acute infections**, the toxins may injure or paralyze the vasomotor center, so that the peripheral arterioles dilate markedly. Thus in typhoid fever, the maximal blood pressure may fall below 70, though in most cases it ranges between 110 and 90 (minimal between 85 and 60). In acute peri
pressures are met with. Indeed, in most acute infections ther
the height of the fever. In lobar pneumonia, the course may
blood pressures, but not infrequently collapse is associated
tension from vasomotor paralysis. In meningitis, there is o
sure, owing to the increased intracranial tension.

In **pulmonary tuberculosis**, the maximal blood pressure
low, say from 20 to 40 mm. lower than in healthy people of

tension is not constantly present, however, and the pressure may vary considerably at different times in the same individual. According to Haven Emerson, the causes are (1) a toxic action on the vasomotor center and (2) a progressive atrophy of the cardiac muscle.

It should be remembered that pleural effusion tends to increase blood pressure, and the blood pressure falls when the fluid is drawn off. The fall amounts ordinarily to 20 mm. of Hg (Capps).

In **surgical shock**, there is a fall of blood pressure. Some believe this to be due to exhaustion of the vasomotor center or of the brain cells, the result of violent sensory stimuli or "noci" impulses (G. W. Crile); others maintain that shock is the result of lack of fluid in the circulation, the total volume of blood being decreased through transudation of fluid into the tissues, this in turn depending upon diminished hemic osmotic tension due to loss of CO_2 from the blood or acapnia (Yandell Henderson). Whatever the explanation of the fall of blood pressure, certain it is that observation of this fall, associated with increase of the heart rate, is the best method of recognizing beginning shock during or after operations. The prevention of acapnia during anesthesia is favored by regulating the amount of CO_2 inspired (Gatch).

In the **cachexias**, in which there is anemia and brown atrophy of the heart, tachycardia and arterial hypotension are nearly always observable.

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7. The Absolute Sphygmogram (Sahli)

The ordinary sphygmogram of an artery (or arteriogram), which is a blood pressure curve in which the heights of the ordinates are indefinite, can be transformed into an absolute sphygmogram by introducing the pulse

curve into a system of ordinates in which the minimal blood pressure i
used as the base, or lowest point, of the pulse curve, and the maximal bloo

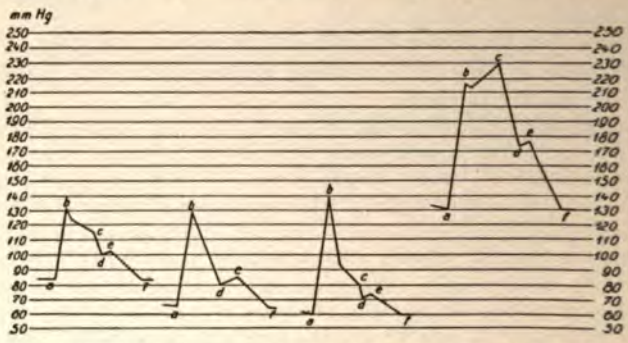

Fig. 235.—Course of the Blood Pressure in the Radial Artery. Blood Pressure Appara
on Upper Arm; Sphygmograph on Wrist. (a-b) Ascending Portion; (b) Top of the Fi
Systolic Wave; (c) End of Second Systolic Wave; (c-d) Post Systolic Fall; (d) Beg
ning of the Dicrotic Wave; (e) Top of Dicrotic Wave; (d-f) Diastolic Portion of
Curve. (After Seifert and Müller, "Taschenbuch d. Medizin—Klin. Diagnostik," p
lished by J. F. Bergmann, Wiesbaden.)

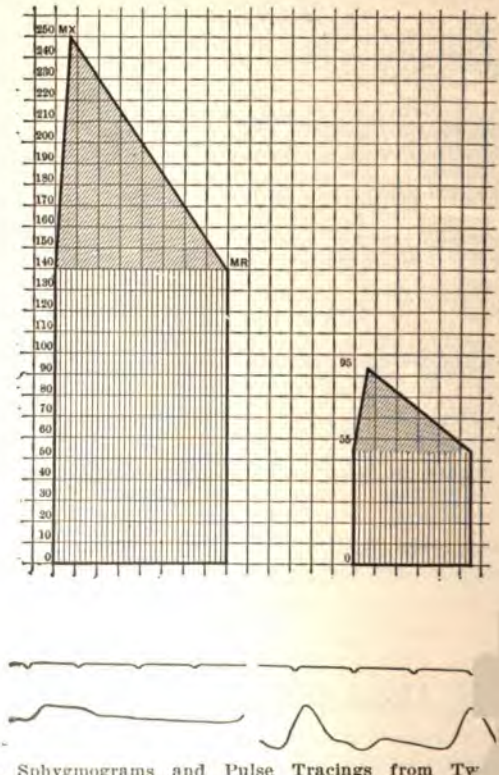

Fig. 236.—Absolute Sphygmograms and Pulse Tracings from Tw
Normal Blood Pressure, One with Nephropathic Hypertension. (
G. W. Norris' "Blood Pressure: Its Clinical Applications," publ
Philadelphia.)

pressure as its highest point; in such a curve, the ordinates now represent the pressures in millimeters of Hg and the abscissae the time in fractions of a second, the whole curve corresponding to the course of the pressure in the artery (Sahli). No attention need be paid to the secondary elevations of the arteriogram, since it is only the rapidity of the ascent and descent of the pulse waves that need be here regarded.

In the absolute sphygmogram, the pulse pressure can be read off directly, since it is the difference between the maximal and the minimal blood pressures. Our best measure of the *tension* of the pulse is the minimal blood pressure.

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8. Determination of Venous Blood Pressure

Many methods have been devised for determining the blood pressure in the veins. Only three of these will be described.

(*a*) *Method of Hooker and Eyster* (*1908*)

Applying a principle utilized by v. Basch and, later, by v. Recklinghausen, Hooker and Eyster place a pressure-chamber over a vein on the front of the wrist and blow in air until the vein "collapses," reading off the pressure at that moment on a water-manometer (see Fig. 237).

Fig. 237.—Apparatus of Hooker and Eyster for Determining the Venous Pressure. (J. H. H. Bull.)

(*b*) *Method of Moritz and v. Tabora* (*1909–10*)

A hollow needle, connected with a buret of normal salt-solution is introduced into the vein at the bend of the elbow (asepsis!), the patient recumbent. The fluid is allowed to run in, its level in the buret gradually falling until flow ceases. The level of the saline above the level of the heart (say a point on the fourth rib, 5 cm. below the level of the surface of the chest) is then read off; the result is the venous pressure at the heart in cm. of normal saline. The calculation in centimeters of H_2O may easily be made, since 10 cm. normal saline equals 10.07 cm. H_2O. The method is believed to be accurate.

(c) *Method of A. A. Howell (1912)*

Two cuffs are used, each being attached to a water manometer. One is applied to the upper arm, the other to the forearm. The latter is inflated so as to fit snugly but without exerting over 3 cm. (H_2O) pressure. The cuff on the upper arm is then cautiously inflated until the water in the forearm manometer begins to rise. The pressure in the upper-arm cuff is equal to the venous pressure.

In a similar instrument, devised by Frank and Reh (1912), the readings may be graphically registered.

9. The Normal Blood Pressure in the Veins

At the level of the heart, the venous pressure varies normally between 1 and 13 cm. of H_2O=0.7–9.5 mm. Hg.

The figures in the bibliography vary a good deal, as will be seen from the following table:

NORMAL VENOUS PRESSURE AT LEVEL OF HEART

Observer	Cm. H_2O	Mm. Hg
Hooker and Eyster.....	3–10 cm. Average 8 cm.	2.2–7.3 mm. Average 5.9 mm.
Moritz and Tabora.....	1.1–8.7 cm. Average 5.2 cm.	0.8–6.4 mm. Average 3.8 mm.
Howell..... ..	4–13 cm. Average 7.6 cm.	2.9–9.5 mm. Average 5.6 mm.

Physiological Variations of Venous Pressure.—The most important factor influencing venous pressure is the *position of a part with relation to the heart.* The pressure in the veins in parts in various positions has been carefully studied and recorded by v. Recklinghausen. The venous pressure rises slightly on *exercise,* and on sudden *changes in temperature.* The venous pressure is but little affected by *changes in arterial blood pressure.* The changes in venous pressure during the *phases of respiration* have been examined by Burton-Opitz, who finds that, during expiration, the pressure in the jugular vein rises; it begins to fall in the pause following expiration and continues to fall in the early part of inspiration.

10. The Venous Blood Pressure in Pa States

As the myocardium begins to fail, blood begins to a systemic circulation and the venous blood pressure is an high venous pressure is associated with a dilatation of t

low venous pressure is associated with insufficient filling of the heart and, accordingly, a decrease in the size of the heart.

In cardiac decompensation, the venous blood pressure may be as high as 25 cm. H_2O in the veins of the arm at the level of the heart (A. A. Howell). After intravenous injections, the venous pressure rises more proportionately than does the arterial pressure (Bayliss and Starling).

A very low venous pressure may be found in neurasthenia and in post-operative asthenia. Cody, working with Hirschfelder in my wards, measured venous pressures in such states as low as -2 to -7 cm. H_2O, though the arterial pressures were not markedly altered, varying as they did between 104 and 125 mm. Hg.

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H. Determination of the Functional Capacity of the Heart

Laudable efforts have been made to test the functional power of the heart or to estimate the work done by the heart, clinically, but the results have been notoriously unsatisfactory. The methods in use try to establish the absolute power of the heart. To calculate the work of the left ventricle, we should have to know (1) the systolic output and (2) the mean pressure in the aorta. But, clinically, these factors cannot be determined accurately, and, moreover, as Külbs emphasizes, if it were possible in some way or another to measure the power of the heart at a given moment, the result obtained, to be of any use, would have to be related to many other coëxistent factors. For the absolute power of the heart is less important than the response of the heart to different somatic and psychic needs and

this response is not only different for different persons but varies extraordinarily in the same person from day to day and from hour to hour. The multiple factors concerned in this variation are still inaccessible to us clinically; probably they are largely neural. It is well for the student to be familiar, however, with the attempts now being made to measure the functional capacity of the heart, for out of them, sooner or later, something of distinctly practical value may emerge.

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As has long been known, the pulse rate increases when work is done by the muscles. The accompanying blood pressure changes during work have recently been systematically studied.

Graupner's Test for Functional Capacity.—This author made certain muscle groups perform a definite amount of work and studied the blood pressure while the work was being done. He believed he could draw conclusions regarding the power of the heart and the peripheral resistance.

The work consisted in the turning of a wheel provided with a brake, and permitting of a measurement of the work done. He concluded that (1) if the blood pressure remained constant, the heart was sufficient for the work; (2) if the blood pressure fell, the heart was insufficient for the work; (3) if the blood pressure rose at first, and then returned to normal, the heart possessed "compensatory capacity"; and (4) if the blood pressure rose, fell rapidly, and did not again tend to rise, the heart was fatigued.

Graupner's method has been controlled by F. Klemperer an
and found unreliable.

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Strasburger's Method of Estimating Functional Capacity.—When the work of the heart increases there is an increase not only of the maximal pressure in the arterial system but also of the pulse pressure and of what Strasburger calls the pulse pressure quotient (pulse pressure divided by mean pressure), commensurate with the increased systolic output; when the work of the heart is lessened, all these factors are smaller. In hypertony of the peripheral arteries the maximal pressure rises, but the pulse pressure (and pulse-pressure quotient) falls. In dilatation of the peripheral vessels the pulse pressure rises but the maximal pressure falls. Thus, when maximal pressure and pulse-pressure quotient are altered in the same direction it is the central component of the blood pressure (systolic output) that is the important factor; when maximal pressure and pulse-pressure quotient alter in an opposite direction, it is the peripheral component of the blood pressure (peripheral resistance) that is responsible. Strasburger goes further and tries to estimate the amount of the work done by the heart from the number of beats, the pulse pressure and the mean pressure. He regards the quotient, pulse pressure divided by maximal (systolic) pressure, as a fair measure of the size of the systolic output on the ground that the relation of the pulse pressure to the blood pressure must show itself. If the pulse pressure were to rise until it equalled the maximal pressure, then this quotient would become 1 and the diastolic pressure would equal 0. These would be, hypothetically, the best conditions for the outflow of blood in the artery, the vascular resistance being very small. In the opposite case, where the above-mentioned quotient is smaller, the outflow of blood would be more difficult, owing to greater resistance in the periphery.

According to Strasburger, the following conclusions may, accordingly, be drawn:

1. When the systolic pressure is altered, the blood-pressure quotient remaining unchanged, the cause is a change in the work of the heart; a rise indicates increased heart work; a fall indicates diminished work.

2. Change in the systolic pressure and in the quotient about equally marked, but in opposite directions, indicates change in the vascular tonicity; rise of systolic pressure and fall of quotient indicate increased vascular tonus; the reverse, depressed tonus.

3. When the systolic pressure and the quotient move in the same or in opposite direction but in unequal degree, there is an alteration both of the vascular tonus and of the work of the heart.

Strasburger's method is unreliable since (1) it ignores the enormous importance of nervous influences, and (2) it tries to draw "dynamic" conclusions from "static" data.

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Erlanger's and Hooker's Method for Estimating Heart Work.—These investigators, working in Howell's laboratory in Baltimore, draw conclusions regarding changes in the work of the heart and of the peripheral resistance from clinical determinations of (1) the maximal blood pressure and (2) the product of pulse pressure multiplied by pulse rate.

TABLE

Changes		Cause	
Maximal Blood Pressure	Pulse Pressure × Pulse Rate	Work of Heart	Resistance
Unchanged.....	{Greater {Less	{Increased {Decreased	{Decreased {Increased
Rise.....	{Unchanged {Greater {Less	{Increased {Increased {Unchanged	{Increased {Unchanged {Increased
Fall.....	{Unchanged {Greater {Less	{Decreased {Unchanged {Decreased	{Decreased {Decreased {Unchanged

This method is subject to the same criticism as has been made of Strasburger's method.

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Müller* (*O.*) & *Vöchting* (*K.*).** *Zur Frage des Herzschlagvolumens. Deutsche Arch. f. klin. Med., Leipzig,* ***1913, *cx, 389–410.*

Katzenstein's Method of Estimating the Functional Capacity of the Heart from the Behavior of the Blood Pressure on Exclusion of Certain Arterial Domains.—The patient is placed in the recumbent posture, and the iliac arteries are compressed for a period of 2½-5 minutes, care being taken to av[illegible] excitement and pain. The work of the heart is increased by this nar[illegible] the arterial bed. Katzenstein found that:

(1) If the heart be normal and sufficient, there is an increase of [illegible] in the blood pressure, the pulse rate remaining unchanged or being [illegible]

(2) If the heart be hypertrophied and sufficient, the blood pressu[illegible] 40 mm. Hg, the pulse rate remaining stationary or becoming slowe[illegible]

(3) If the heart be slightly insufficient, the blood pressure rem[illegible] the pulse rate unchanged or plus; and

(4) If the heart be markedly insufficient, the blood pressure falls and the pulse rate is accelerated.

Here, again, it is almost impossible to exclude the psychic factors that influence the heart and the arteries; and the results obtainable are of doubtful clinical value.

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Zuntz and Plesch's Method of Estimating the Functional Capacity of the Heart, Based upon Calculations of the Systolic Output.—The systolic output is calculated from the difference in the oxygen in the arterial and the venous blood and from the oxygen-intake during respiration. First, the oxygen-content of the blood taken from an artery is determined by the colorimetric method of Plesch (*q. v.*). The oxygen-content of the blood in the right ventricle is judged by the O_2-tension in the residual air of the lungs, since the two stand in equilibrium. Plesch determines the O_2-tension by allowing the patient after a deep inspiration to exhale and inhale several times, using a balloon containing a definite amount of nitrogen. Subsequently, he determines the oxygen used per minute with the Zuntz-Goeppert respiration apparatus. The minute-volume contains the amount of oxygen that is taken up on respiration; it is equal to the difference in total oxygen-content of the arterial blood and of the venous blood that flows through the lungs during one minute. Now if the minute-volume of the heart be divided by the pulse rate per minute, we get the "systolic output."

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Sahli's Sphygmobolometry.—Sahli attempts to get at the functional power of the heart indirectly by estimating the energy of the single pulse waves. For this purpose, he has devised a special instrument, the sphygmobolometer. This instrument is not difficult to use, and the necessary observations can be made in a few minutes.

The normal amount of energy of the brachial pulse wave is usually between 40 and 60 g/cm. In pathological states, these values may be doubled. For the technic, Sahli's descriptions should be consulted.

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Christen's Energometry.—The energometer of Christen consists of a cuff, which is applied to the calf of the leg or the upper arm, a special manometer, a pump, and a syringe with piston—all connected with one another. By means of the pump, a definite pressure is produced within the cuff, after which the pump is clamped off and the excursions of the tonometer needle noted. Enough air is now injected into the cuff with the syringe to displace the oscillations of the tonometer needle by about their own amplitude, that is, so that the needle at every pulse beat oscillates between two limits, of which the lower had been (before the air was injected) the higher limit of the oscillation. The volume of air used for this purpose is read off on the scale of the syringe; it is equal to the systolic increase of volume of the arteries under the inflated cuff. By multiplying this volume by the mean pressure within the cuff, one obtains the "work" in gram-centimeters performed by the pulse wave. Such a measurement can be made for a series of different pressures within the cuff; in each instance, the energy (E) is equal to the pressure (P) multiplied by the volume (V); that is, $E = PV$.

By plotting these pressures and their corresponding volumes in one curve, and the pressures and their corresponding energies in another curve, we get two curves known as "dynamic diagrams," which represent the volumes and the energies as functions of the pressure. In drawing the curves, the pressures are plotted as abscissae, and the volumes and energies as ordinates.

The dynamic curves may be characteristic in certain pathological states, especially in aortic insufficiency, in arteriosclerosis, and in cachectic states.

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The method of Sahli and that of Christen are of co for research work. It is too early, as yet, however, to they will prove to be in practical clinical work.

Attempts such as the above to determine changes

heart and the peripheral resistance are laudable; but we deal here with such complicated relations that too much stress should not be laid, as yet, upon the results that they yield. The time may come when we shall be able to attain more nearly than we can at present to the ideal toward which this work tends. In atherosclerosis and in valvular diseases of the heart, especially, efforts at determination of the work of the heart based upon blood-pressure measurements are liable to error.

SECTION II

DIAGNOSIS OF THE SPECIAL DISEASES OF THE HEART AND BLOOD VESSELS

The circulatory system, like the other systems of the body, is susceptible to a variety of diseases. Those involving the heart include:

(1) Disturbances of development (*congenital heart disease*).

(2) Retrogressive disturbances of nutrition (*atrophies* and *degenerations*).

(3) Circulatory disturbances (*infarctions, thromboses, diseases of the coronary arteries, aneurism of the heart*).

(4) Inflammations of the heart as a whole (*carditis*), of the lining membrane of the heart (*endocarditis*), of the heart muscle (*myocarditis*) or of the pericardium (*pericarditis*). These inflammations give rise to *acute inflammatory cardiopathies* and, later on, to *chronic inflammatory cardiopathies.*

(5) Reparative and adaptive processes in the heart (*hypertrophy, dilatation*).

(6) Alterations in the position and shape of the heart.

(7) Foreign bodies and parasites in the heart.

(8) Tumors of the heart.

Only the more important of these can be considered here. For the others, special monographs should be consulted.

Before proceeding to the more systematic study of the diseases of the heart, certain gross disturbances of cardiovascular function must be discussed, namely, (1) Certain Clinical Disorders of the Heart Beat and (2) Acute and Chronic Circulatory Insufficiency.

A. Clinical Disorders of the Heart Beat

1. Introduction

Among the commonest of clinical phenomena met with are derangements of the rate, sequence, and force of the heart beat. They include the tachycardias, the brady- arhythmias, and the alternating heart. The analysis of

has made great progress since 1870. We owe the progress partly to advances in experimental physiology, partly to careful clinical studies, especially those involving the use of graphic methods (sphygmography, electrocardiography).

The functions of the cardiac musculature include (1) the power of initiating primary stimuli at regular intervals (automatic rhythmicity), (2) the power of responding to stimuli (excitability), (3) the power of conducting stimuli (conduction capacity), (4) the power of contractility. Influences, neural or other, that affect these several functions, have been given special names. Thus, influences affecting the automatic rhythmicity are known as **chronotropic**; those affecting the excitability, as **bathmotropic**; those affecting the conductivity, as **dromotropic**; and, finally, those affecting the contractility, as **inotropic.**

Methods of graphic registration are of great importance in the unravelling of the mysteries of cardiac irregularities. They further afford us a means of checking, and consequently of improving, our ordinary methods of physical diagnosis in these types of cases. Working with Drs. Hirschfelder, Bond, and Bridgman, I have had manifold opportunity during the past ten years to convince myself of the great clinical value of these methods. Arteriograms and phlebograms should always be taken simultaneously for comparative study, in analyzing any form of irregularity, though, when electrocardiograms are available, the sphygmographic tracings may usually be dispensed with. Most of the beautiful electrocardiograms that illustrate this section of the book were taken by Dr. George S. Bond in the Heart Station at the Johns Hopkins Hospital; a few of them were taken by Dr. Bridgman.

For analysis of the curves obtained, the various forms of cardiac arhythmia may be grouped under different headings, depending upon the causal factors that produce each one.

2. Classification of the Cardiac Arhythmias

The following classification serves as a good working basis:

I. Sinus irregularities.

(a) Phasic variations in rate.
  1. Associated with respiration.
  2. Not associated with respiration.

(b) Dropped beats.

II. Abnormal impulses arising in the heart.

(a) Extrasystoles

2. Atrial (or auricular).
3. Nodal.

(b) The paroxysmal tachycardias.
(c) Atrial (or auricular) fibrillation.
(d) Atrial (or auricular) flutter.

III. Changes in contractile force.

(a) Pulsus alternans.

IV. Disturbances in the conduction system in the heart (heart block).

(a) Disturbances of the atrioventricular conduction-path.
1. Slowed conduction.
2. Partial block.
3. Complete block.

(b) Disturbances of the intraventricular conduction-path.

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3. Common Examples of Cardiac Arhythmia

A rough idea of the majority of these disturbances can be quickly arrived at by any general practitioner who will appeal to his personal experience in palpating the pulse of patients. Thus, (1) he will recall that on feeling the pulse of young persons, he has often noticed a difference in the pulse rate in the two phases of respiration; this is an example of a *sinus arhythmia.* He will remember (2) instances in which the pulse occasionally intermits, and on listening over the heart he will have noticed that such an intermittence is associated with a cardiac contraction occurring before a regular beat is due and that this early contraction is followed by a pause longer than the ordinary pause between two beats; this is an example of a *premature beat,* or so-called *extrasystolic irregularity.*

Again, he may recall (3) instances in which the pulse of a patient has suddenly doubled its rate; the rapid pulsation has continued for a time, and has then abruptly ceased. The patient complains that such attacks of rapid heart recur from time to time; this is an example of *paroxysmal tachycardia.*

Occasionally, he may encounter (4) an elderly person in whom the pulse rate is continuously accelerated (120-160 per minute) though there is no exophthalmic goiter, and the pulse is not irregular; such a tachycardia is usually due to *atrial* (or *auricular*) *flutter.*

More often, he will have noticed (5) in patients who have long suffered from disease of the mitral valve, the onset of a "perpetually irregular pulse," an "utterly disordered heart action," in which the pulse rate is accelerated, but there is no regularity of sequence of the beats whatever, and the patient shows signs of cardiac decompensation; this clinical picture is characteristic of *atrial* (or *auricular*) *fibrillation.*

In some patients, especially in those with high blood pressure, he may have noticed (6) that the pulse beats at the wrist, though rhythmical, vary in force, the beats being alternately strong and weak; this is an example of *pulsus alternans.*

Finally, he may have seen (7) one or more patients at the wrist is regular but only 30 or 35 per minute, th the jugular vein in the neck, three or four small regular to occur between two carotid pulses; this is an example *block.*

Such typical disturbances are recognizable withou methods, but, in clinical work, we often have to unr

are far less differentiable, and then we must resort to sphygmography, to electrocardiography, or to both, to arrive at a satisfactory diagnosis. The simple examples given above may serve as paradigms for the classes of disturbances now to be considered.

4. Sinus Irregularities

(*a*) *Phasic Variations in Rate*

The small portion of tissue at the junction of the superior vena cava with the right atrium (the so-called "sinus region") is the point at which the cardiac rhythm normally originates, and this sino-auricular node (Keith and Flack) has been termed "the pacemaker of the heart" (T. Lewis.) The rapidity at which the stimulus to cardiac contraction is initiated at this point is subject to the controlling influence of the vagus and the sympathetic nerves. In normal adults, the balance between the inhibiting or slowing influence of the vagi and the accelerating influence of the sympathetic is well preserved, and the heart rate remains constantly about 72 when a person is at rest. In children, however, or in adults whose nervous systems are unstable from any cause (infections, toxemias, etc.), the heart rate will fluctuate with every change of vagal tone. This is most often associated with the phases of respiration, but, occasionally, the change in rate may have no relation to respiration as in the *youthful irregularity* (Mackenzie).

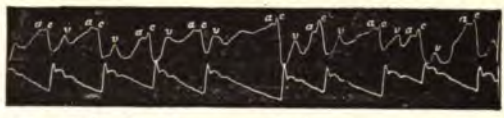

Fig. 238.—Phlebogram and Arteriogram in the Youthful Type of Irregularity. (After J. Mackenzie, J. H. H. Bull.)

The arteriograms, phlebograms and electrocardiograms in this form of irregularity all present characteristic features. (Fig. 238). This form of arhythmia is easily recognized by the periodic variation in the rate of the heart when a rather long stretch of a sphygmographic or an electrocardiographic curve is examined. There is first a series of beats in which diastole becomes longer and longer, and this is followed by a series of quickened beats with shortened diastole. When the arhythmia is associated with the phases of respiration **(pulsus irregularis respiratorius)** the longer intervals between beats usually occur during expiration and the shorter ones during inspiration. Most irregularities of the heart in chil-

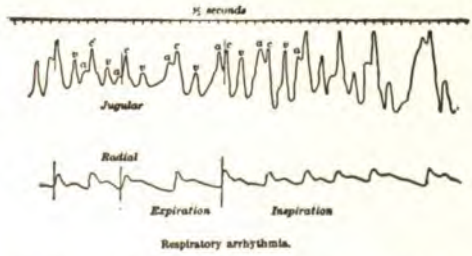

Fig. 239.—Phlebogram and Arteriogram in Pulsus irregularis respiratorius. (After A. W. Hewlett, J. H. H. Bull.)

dren before puberty are sinus arhythmias. These arhythmias disappear if the heart rate be accelerated by exercise, by fever, or by the administration of drugs, like atropine, that paralyze the vagus.

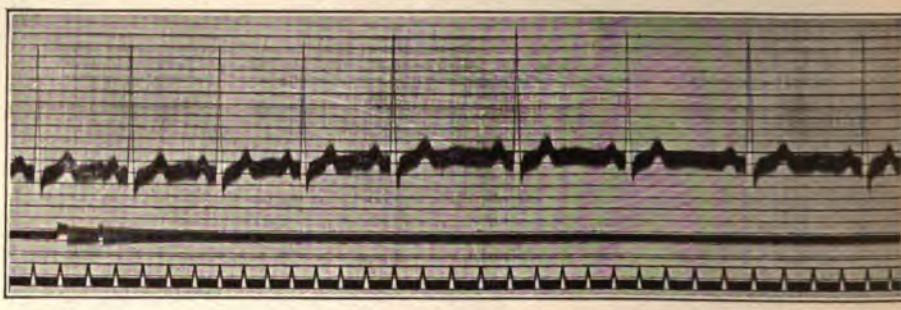

Fig. 240.—Electrocardiogram in Sinus Arhythmia. Respiratory Form. Note the Marked Variation in Rate with the Phases of Respiration. There is no Change in the Form of Contraction of the Heart, as is Shown by the Normal Type of Electrocardiographic Curve.

(*b*) *Dropped Beats*

This is another form of sinus arhythmia, occasionally met with. It may also be due to vagus inhibition, or it may result from an actual change in the sinus region itself. It is characterized by a complete absence of

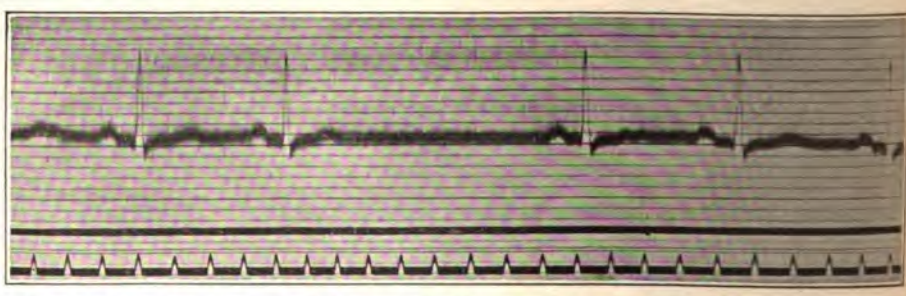

Fig. 241.—Electrocardiogram of Dropped Beats. As Shown in this Electrocardiogram, a Complete Cardiac Contraction is Missing in a Rhythm, Otherwise Normal. This may be Due to a Sino-auricular Block, or to Lack of Stimulation in the Sinus Itself.

contraction of the whole heart (standstill) for a period lasting through one or more cardiac revolutions. All forms of graphic registration point out that the entire heart is quiescent during this pause (Fig. 241).

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5. Arhythmias Dependent upon Abnormal, Premature Impulses Arising in the Heart

(*a*) *Extrasystolic Arhythmias*

Normally when an impulse originates in the "pacemaker," it passes, thence, in regular sequence, through the other cardiac chambers. This regular order is due to the fact that each succeeding portion of the heart muscle traversed by the impulse has an independent rhythmicity, which is slower than that of the preceding one, and, consequently, it receives a stimulus conducted from above and responds to it before it can initiate its own automatic impulse and contraction. However, when the irritability of any part of the heart is increased, it may release a spontaneous contraction, itself, before it receives a regular stimulus from the superior part. This phenomenon has been termed "heterogenetic beat," a "premature contraction," or "an extrasystole." Such new and isolated impulses may originate in any portion of the cardiac musculature—in the atria, in the ventricles, or in any part of the conducting system between the atria and the ventricles. They are classified, according to their point of origin, as (1) atrial, (2) ventricular, and (3) nodal extrasystoles. Such extrasystolic contractions of the heart, occurring before the regular, normal time, disturb markedly the normal order of the mechanism of the heart.

i. Ventricular Extrasystoles

The term "ventricular extrasystole" is applied to a premature beat when it arises in the wall of one of the ventricles. The connection, however, between the two ventricles is so intimate that, regardless of where this abnormal stimulus may originate, both ventricles take part in the premature contraction. Usually, the regular rate of the atrial rhythm is not disturbed by the ventricular action, and atrial systole occurs during, or just after, the premature systole of the ventricles. In consequence of the latter, the ventricle is unable to respond to the impulse conducted from the atrium

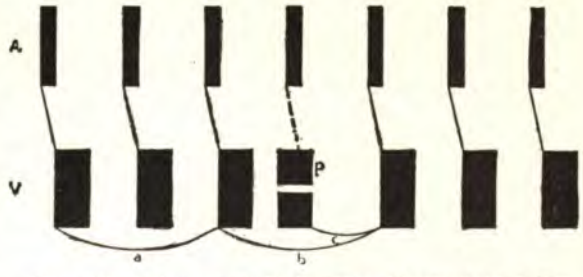


Fig. 242.—Diagram of Disturbance Produced by a Ventricular Extrasystole (*p*). Note that the Atrium Beats Regularly Throughout. The Ventricle Responds to Six Atrial Impulses, but the Impulse of the Atrial Systole in the Center of the Diagram is Lost, for it Falls while the Ventricle is in Premature Systole. The Break in the Center of the Ventricular Beat Indicates its Abnormal Origin. Note that the Lengths of Periods (*a*) and (*b*) are Equal, while Period (*c*) is the "Compensatory Pause." (From T. Lewis, "Clinical Disorders of the Heart Beat," published by P. B. Hoeber, New York.)

until the succeeding atrial contraction, and there thus results a delay in the ventricular rhythm following the premature beat. It is known as the **compensatory pause,** because the time occupied by (1) the beat preceding the premature beat, (2) the premature beat itself and (3) the pause following it, just equals the time of two regular cardiac cycles. If the extrasystole occurs very early and the atrial rate is slow, the ventricle may be able to respond to the first regular atrial stimulus succeeding it. In that event, the extrasystole is a true extra beat in the ventricular rhythm, and is known as an **interpolated extrasystole.**

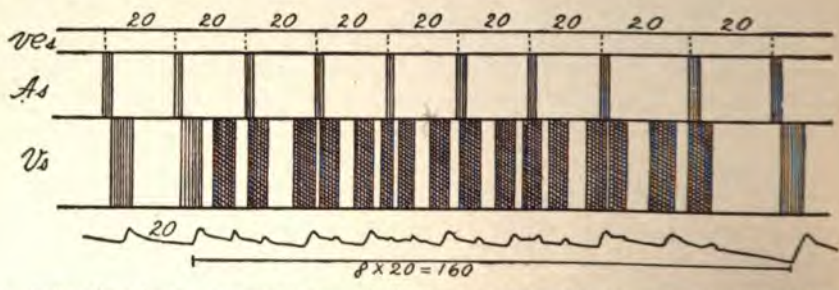


Fig. 243.—Ventricular Extrasystoles. (After K. F. Wenckebach, "Arch. des Maladies du cœur," published by Baillière et Fils, Paris.)

Pulse Tracings Illustrating Ventricular Extrasystoles (Fig. 243).—The premature ventricular contraction, as well as the lengthened diastolic pause that follows it, are easily recognizable on the cardiogram of the apex beat.

In the arteriogram of the carotid or of the radial pulse, the premature contraction may or may not be represented by a wave, depending upon the strength of the extra-contraction and the amount of blood it has forced into the aorta. Thus, there may be only a long pause of two cardiac revolutions, or the extrasystole may be marked by a small arterial wave, occurring early and followed by the compensatory pause.

The phlebogram or jugular tracing shows a single wave coincident with

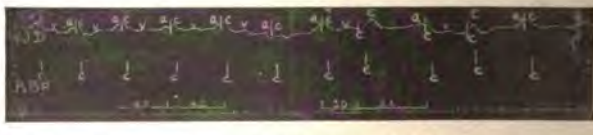
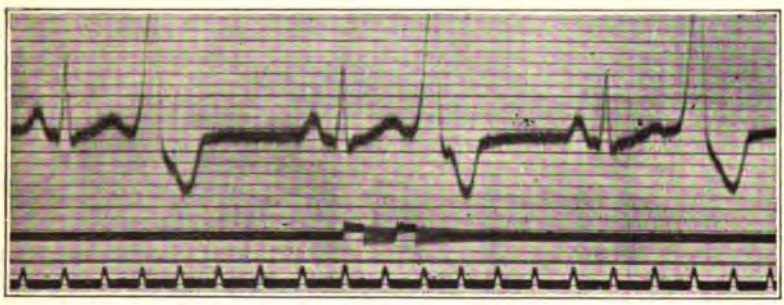


Fig. 244.—Ventricular Extrasystoles. Extrasystole Shown at E, No *a*-Wave Precedes. (Tracing by Dr. A. D. Hirschfelder, J. H. H. Bull.)

the extrasystole, and not preceded by an atrial *a*-wave. When the regular atrial systole occurs simultaneously with the ventricular extrasystole, the single wave on the phlebogram is very large; it represents a combined venous impulse from both the atrium and the ventricle, and, in it, the atrial element is magnified, because the atrium has contracted against

a closed ventricle. Such sphygmographic evidence is sufficient for the decision that an extrasystole has originated in the ventricles, but the electrocardiogram permits of still further analysis and differentiation.

Electrocardiograms of Ventricular Extrasystoles (Fig. 245).—This electrical method of registration also points to the features observable by the other methods just described. Thus, one sees a wave representing the early ventricular systole. It is not preceded by an atrial wave (*P*), but it is followed by a compensatory pause. Furthermore, the wave due to the premature contraction itself does not assume the usual ventricular type (*Q-R-S-T complex*) but is of an anomalous form. In explaining this difference, one must remember that, in the normal heart beats, all parts of the ventricular system contract nearly simultaneously, while in the ventricular extrasystole, the abnormal stimulus arises at some point in either the right or the left ventricle, and is thence propagated to the remaining parts as a wave of stimulation and contraction. This extrasystolic type of ventricular



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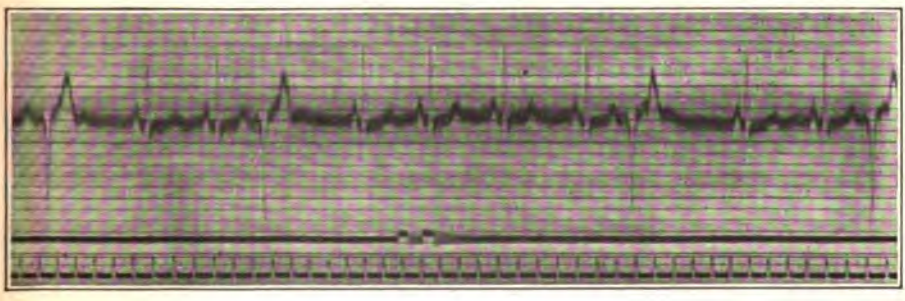


II

Fig. 245.—Electrocardiograms of Ventricular Extrasystoles. The Ventricular Extrasystole is Shown by an Electrical Curve that is Entirely Different from that Produced by a Normal Cardiac Contraction. The Wave is a Single, Large, Diphasic Form, which Indicates that it is Probably More Like a Wave of Contraction, than Like a Single Contraction of All Parts of the Muscle Simultaneously.

The Direction that the First Part of the Extrasystole Curve Takes, Indicates the Ventricle in which it Originated. Thus:

I. The Electrical Curve Goes Up First, and Means that the Contraction Started in the Right Ventricle.

II. This Curve Goes Downward First, and Means that it Originated in the Left Ventricle.

contraction, therefore, produces electrical variations in the form of a large diphasic wave, which consumes about the same period of time in the electrocardiogram as the normal ventricular complex. The initial direction of this atypical wave is an indication of the portion of the ventricles first contracting, and permits us to differentiate between extrasystoles beginning in the right from those beginning in the left ventricle. If the diphasic wave be first upward and then downward, it denotes that the extrasystole originated in the right ventricle; while if the wave be first downward and then upward, it originated in the left ventricle.

Patients who suffer from extrasystolic irregularity of this type may complain of "palpitation," of a feeling "as though the heart turned over in the chest," or they may notice the long pause following the premature beat and be uneasy about it. The prognostic importance of ventricular extrasystoles depends upon the conditions with which they are associated; these may be either benign or grave, and, in each case, the condition of the heart and other organs should be carefully studied before prognostications are made.

ii. Atrial (or Auricular) Extrasystoles

This term should, strictly speaking, be applied only to those instances in which there is an early atrial systole and no associated ventricular contraction following it. However, the term is used most frequently in another sense, namely, to designate what is in reality an atrioventricular extrasystole, because though the abnormal impulse arises in the atrium it is also conducted to the ventricle, which as a rule responds to it by a contraction that succeeds the atrial contraction (Fig. 247).

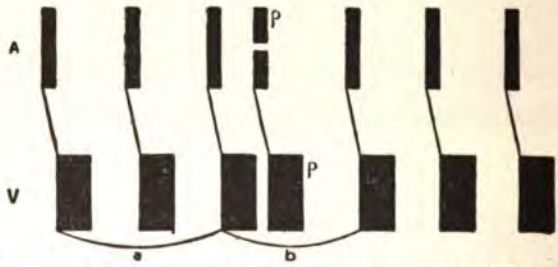


Fig. 246.—Diagrammatic Representation of an Atrial Extrasystole. The Atrial Rhythm is Disturbed by the Abnormal and Premature Atrial Beat (*p*); the Disturbance in the Ventricular Rhythm is Parallel, for Each Atrial Systole Yields a Ventricular Response. The Rhythm of the Whole Heart is Dislocated, the Period *a* being Longer than the Period *b*. (From T. Lewis, "Clinical Disorders of the Heart Beat," published by P. B. Hoeber, New York.)

Pulse Tracings Illustrating Atrial Extrasystoles (

patients manifesting atrial (or auricular) extrasystoles, and arteriograms show a disturbance of rhythm, due to th tricular contraction that is a part of the extrasystole. tole may be followed by a long pause, but the whole turbance is not equivalent, as in the case of ventricular two full cycles of normal cardiac rhythm.

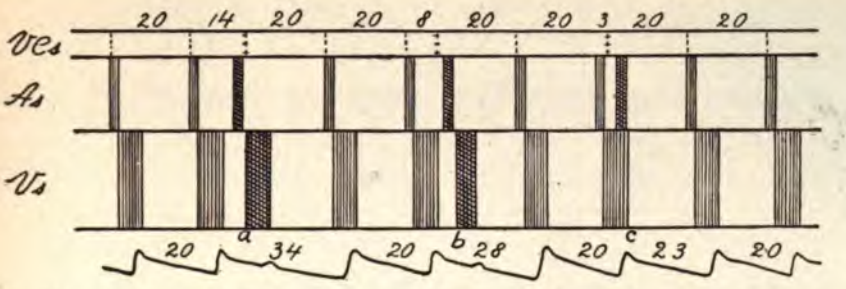


Fig. 247.—(*a*) Extrasystole Arising in the Atrium or Auricle; (*b*) Extrasystole Arising in the Sinus. (After K. F. Wenckebach, "Arch. des Maladies du cœur," published by Baillière et Fils, Paris.)

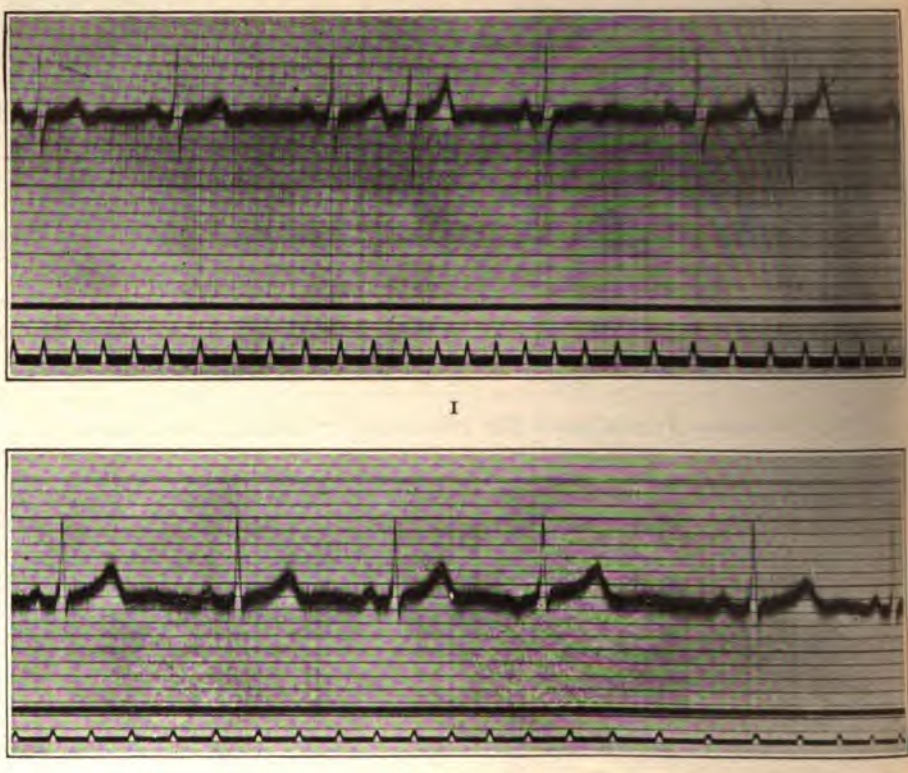
Simultaneous tracings of the venous pulse and of the arterial pulse easily differentiate this form of extrasystole. The phlebogram associated with the premature beat consists of the normal double pulsation made up of the *a*-, *c*-, and *v*-waves, but the distinguishing feature is the presence, in the extrasystole, of the atrial (*a*-) wave that indicates its origin.

Fig. 248.—Atrial Extrasystoles. (Tracing by A. D. Hirschfelder, J. H. H. Bull.)

Electrocardiograms of Atrial Extrasystoles (Fig. 249).—In an electrocardiogram, the atrial extrasystole is revealed simply by the occurrence, prematurely, of a cycle of the normal form, all of the waves *P*, *R*, and *T*, being present in ordinary sequence. In the premature beat, the atrial wave (*P*) is subject to variations in form, depending upon the part of the atrium in which the abnormal stimulus originates. If the extrasystole arise at or near the sinus region, the *P*-wave will be of the same type as the atrial waves of the remaining regular contractions. Should it originate, however, at any other point in the atrial tissue, the *P*-wave will be modified in form. This change is now utilized, clinically, more accurately to localize the site of origin of atrial extrasystoles.

iii. Nodal Extrasystoles

By nodal extrasystoles are meant premature beats that have their point of origin in the conduction system between the atria and the muscular wall of the ventricles, that is, especially in the node of Tawara in the atrioventricular bundle of His. From this point, the stimulus spreads in both directions, retrograde to the atria or auricles and downward to the ventricles, so that atria and ventricles contract almost simultaneously.



I

II

Fig. 249.—Electrocardiogram of Atrial or Auricular Extrasystoles. I. Arising At or Near the Point of Origin of the Normal Stimulus. This is Shown by the Fact that the *P*-Wave that Starts Each Extrasystole is of the Same Form as the Normal *P*-Wave. In this Case it is Superimposed upon the *T*-Wave of the Preceding Contraction, and Increases the Height of that Wave. II. Arising at Some Other Point in the Auricles than the Normal Point. The *P*-Wave of the Extrasystole is Inverted, which Means that the Contraction of the Auricle was Different in Form from that of the Normal Beats in the Same Tracing.

Often, however, there is no evidence of an atrial contraction on the curves, in which event it is impossible to rule out an extrasystole originating rather high up in the conducting system below the node.

Pulse Tracings of Nodal Extrasystoles (Fig. 250).—In cardiograms, arteriograms and phlebograms the picture is like that of a ventricular

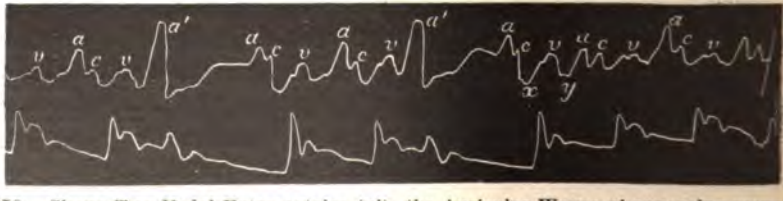


Fig. 250.—Shows Two Nodal Extrasystoles (*a'*), the **Auricular Waves** *a'* **appearing prematurely** and at the same time as the extrasystole **in the radial. (After James Mackenzie,** "Diseases of the Heart," published by Oxford Press, London.)

extrasystole, though, in the jugular tracing, the atrial *a'*-wave may be distinguished as a premature wave synchronous with the extrasystole in the radial pulse.

Electrocardiograms of Nodal Extrasystoles (Fig. 251).—The electrocardiographic method affords the best means of differentiating this nodal type of extrasystole from that of ventricular origin. In place of the

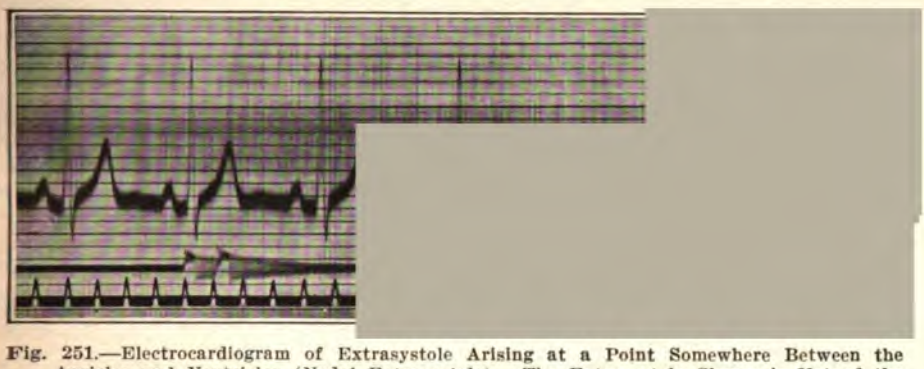


Fig. 251.—Electrocardiogram of Extrasystole Arising at a Point Somewhere Between the Auricles and Ventricles (Nodal Extrasystole). The Extrasystole Shown is Not of the Auricular Type, for it is Not Preceded by a *P*-Wave. (The *T*-Wave of the Contraction Before it is Not Different from those of the Other Normal Beats, and for this Reason is Probably Not a Combination of *P* and *T*.) Neither is it of the Form Usually Seen in Ventricular Extrasystoles. In Form it is Much Like the Normal Ventricular Complex, which Indicates that a Large Portion of the Internal Conduction-Mechanism Entered into its Production. This Means that the Abnormal Stimulus Must have Begun High Up in the Bundle and was Transmitted to the Ventricle in the Normal Manner.

large diphasic wave of the ventricular extrasystole, the premature beat of nodal origin gives electrical variations that are more of the form of the normal ventricular complex. This would indicate that a large portion of the internal ventricular musculature must have been included in the abnormal contraction, and, therefore, the stimulus must have originated very high in the atrioventricular conduction-system. The determination of the presence of a *P*-wave on the curve is often quite uncertain, so that it is not always possible to say that retrograde stimulation (and contraction) of the atrium has occurred.

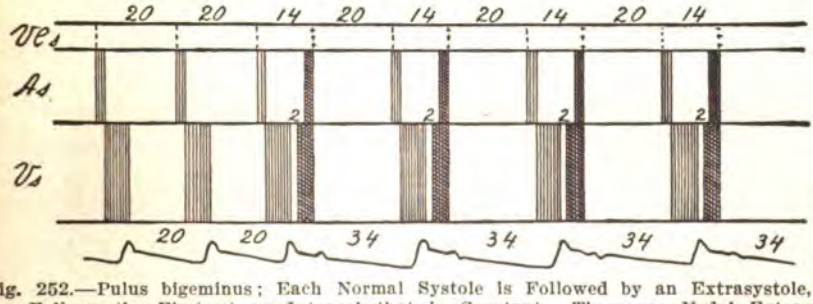


Fig. 252.—Pulus bigeminus; Each Normal Systole is Followed by an Extrasystole, which Follows the First at an Interval that is Constant. These are Nodal Extrasystoles. (After K. F. Wenckebach, "Arch. des maladies du cœur," published by Baillière et Fils, Paris.)

In all types of extrasystolic irregularity the occurrence of the premature contractions may follow a regular sequence in relation to the normal rhythm. Thus, an extrasystole may succeed each regular systole, giving rise to a "coupled beat" or "pulsus bigeminus" of extrasystolic origin. Or two extrasystoles may follow each regular beat, in which case we speak of a "triple beating" or "pulsus trigeminus." It should not be forgotten that "coupled beats" and "triple beating" are not always extrasystolic in origin; they may also be met with in heart block (*q. v.*).

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(*b*) *The Paroxysmal Tachycardias*

These peculiar forms of cardiac activity also indicate abnormal impulse formation in some part of the heart. Just as the atria and the ventricles are capable of producing, when in a state of [illegible] premature contraction in spite of the predomin[illegible] can initiate a prolonged series of abnormal beats [illegible] cardia. In such forms of tachycardia, the onset, [illegible] the attack is very abrupt, and this accounts for [illegible] mal"; this feature distinguishes them from other [illegible] of Graves's disease, of atrial flutter and of atrial [illegible]

paroxysmal tachycardias may be divided, according to the place of origin of the abnormal rhythm, into *atrial, ventricular,* and *nodal* tachycardias.

The heart rate varies between 110 and 200; usually the rate is somewhere between 140 and 190 per minute. One should not rely on the pulse count at the wrist, but should count the heart rate with the aid of a stethoscope. An attack may last from a few seconds to several days; I knew one young man whose attacks lasted for two weeks at a time. It may occur at any age. One of my patients, now over 80 years old, has had attacks since early childhood.

An interesting point in diagnosis is that the heart rate does not change when the patient passes from the standing to the recumbent position.

Pulse Tracings and Electrocardiograms in Paroxysmal Tachycardia (Figs. 253, 254, 255, 256).—If the reader will remember that this condition represents merely a series of atrial, ventricular or nodal extrasystoles that follow one another in rapid, regular sequence, and that these impulses arise in a single focus at some distance from the normal pacemaker, it will be unnecessary further to discuss the form of the curves obtained by graphic methods. The atrial form of paroxysmal tachycardia is the commonest type; it shows a rapid repetition of the features that characterize the individual atrial extrasystole. In the same manner, the ventricular form of paroxysmal tachycardia is characterized by the rapid recurrence of ventricular extrasystoles, and the nodal by the rapid recurrence of nodal extrasystoles.

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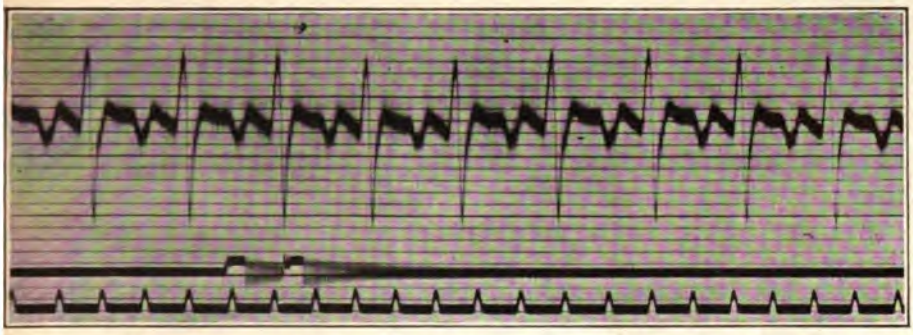

Fig. 255.—Electrocardiogram in Paroxysmal Tachycardia. Atrial or Auricular Type. Rate 170 per Minute. The Rapid Rate is Shown by the Shortened Diastole, the Auricular Wave Falling upon the Final Wave of the Preceding Contraction. There is an Inverted *P*-Wave, Beginning Each Contraction of the Heart. This Indicates that the Tachycardia Arises in the Atria (Auricles), but at Some Part Other than at the Normal Point of Origin.

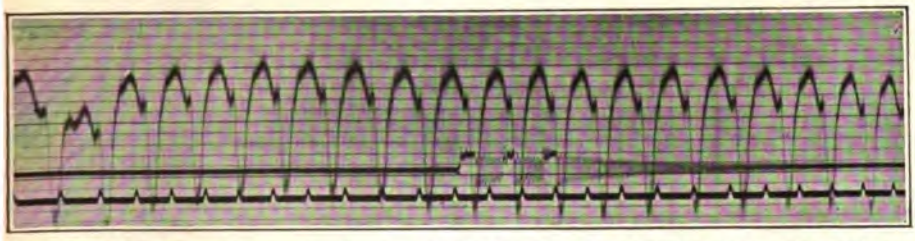

Fig. 256.—Electrocardiogram in Paroxysmal Tachycardia. Ventricular Type. Rate 230 per Minute. This Form Consists of a Series of Ventricular Extrasystoles Following Each Other in Rapid Succession. There is no Sign of any Atrial or Auricular (*P*) Waves to be Seen. The First Part of the Wave of Ventricular Contraction is Downward, which Indicates that the Left Ventricle Contracts First.

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(*c*) *Atrial* (*or Auricular*) *Fibrillation*

One of the most common forms of cardiac irregularity met with clinically is that in which the ventricular action shows a gross disturbance of its rhythm. The ventricular contractions follow one another in disorderly fashion and show marked differences in the amount of force expended. To this form of disturbance of rhythm have been given the

names: *absolute arhythmia, perpetual arhythmia,* and *pulsus irregularis perpetuus.* Clinically, the disorder is characterized by phenomena dependent upon (1) virtual paralysis of the atria, and (2) persistent irregularity of the ventricles. It is only in recent years that it has been demonstrated that this condition is associated with an abnormal form of contraction of the atria, known as **atrial (or auricular) fibrillation.** The muscle of the atria, after a long period of stress, may cease to contract as a co-ordinate unit and the individual muscle-bundles then begin to contract independently of one another. These independent contractions originate at multiple foci in the atria, and some are ocurring throughout the entire cardiac cycle. The stimuli, arising at all these points in the atria, are conducted in a "rapid and haphazard" way to the ventricles, and, thus, the ventricles are continuously bombarded with stimuli of varying strength; to these they respond at irregular intervals. The times of the ventricular contractions depend upon the relations between the strength of stimuli received and the time interval after preceding ventricular contractions.

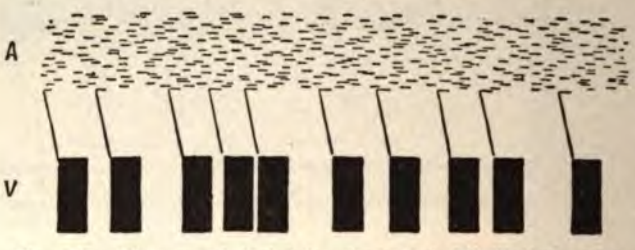


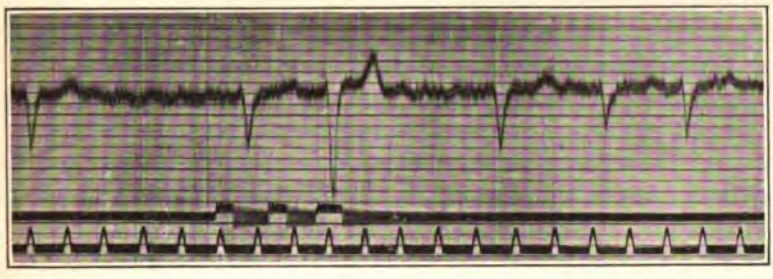
Fig. 257.—Diagram of Atrial (or Auricular) Fibrillation. The Fibers of the Atria do not Contract Coördinately or Together. There are Multiple Foci in which Stimuli Originate. Occasionally, at Very Irregular Intervals, Impulses Leave the Atria and Stimulate the Ventricles; Hence the Rapid and Absolutely Irregular Pulse. (After T. Lewis, "Clinical Disorders of the Heart Beat," published by P. Hoeber, New York.)

Pulse Tracings in Atrial Fibrillation (Fig. 258).—Arteriograms and cardiograms show that the ventricular contractions are of increased frequency, and are very irregular in force and in rhythm.

The venous pulse as studied in phlebograms is found, usually, to exhibit a single, broad wave coincident with each ventricular systole; it is the so-called "ventricular" or "positive" venous pulse (*q. v.*). The absence of the normal atrial contraction is shown by the absence of the *a*-wave, and, in a few instances, the fact that the atria are fibrillating is evidenced by small undulations in the diastolic pauses.

Fig. 258.—Phlebogram and Arteriogram in Pulsus irregularis perpetuus with Atrial Paralysis. (Personal Observation, J. H. H. Bull.)

Electrocardiograms in Atrial Fibrillation (Fig. 259).—The electrocardiographic method of registration yields a very striking and characteristic picture in this condition. A ventricular complex (*R*- and *T*-wave) marks each ventricular contraction, and the unequal spacing of the ventricular complexes certifies to the irregularity of the ventricular rhythm. The ventricular complex often shows variations in form in successive beats, an indication that the ventricles do not always contract in the same man-



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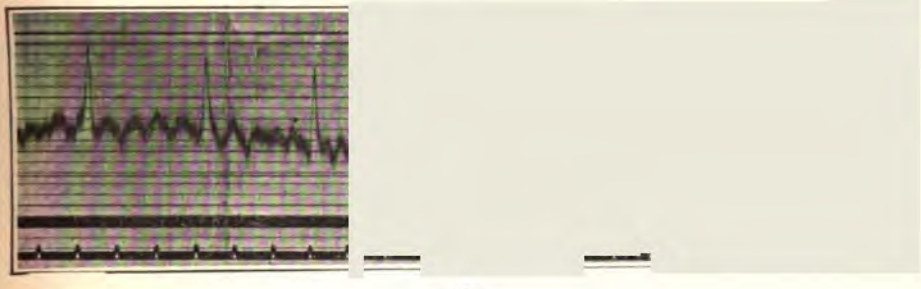

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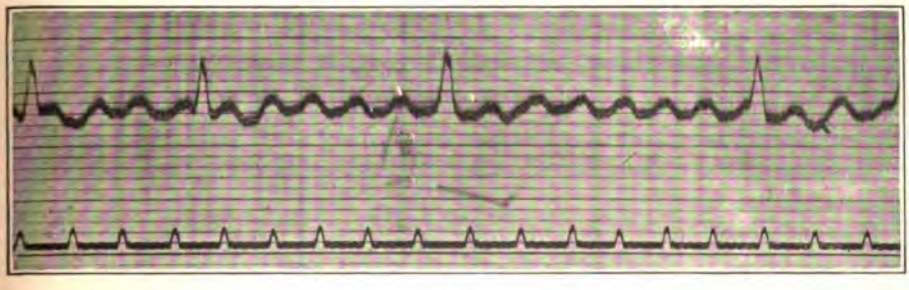

C

Fig. 259.—Electrocardiograms in Atrial (or Auricular) Fibrillation and Flutter. In Auricular Fibrillation and Flutter the Main Features are, Complete Absence of the *P*-Wave, Marked Irregularity of the Ventricle (Shown by the *R*-Wave), and an Almost Constant Vibration of the String, Caused by the Fibrillating Auricle. A, Fine Type. Here the Waves are Small and Very Rapid. B, Coarse Type. The Waves in this Form are Much Larger and Slower. The Fibrillation Waves Vary Greatly in Size and Form, as well as in Time. C, Auricular Flutter. In this we See a Distinct Regularity in Size, Form, and Time of the Auricular Oscillations.

ner. The atrial wave (*P*), seen in the electrocardiogram of the normal heart, is here absent because there is no distinct coördinated atrial contraction. It is replaced by many small oscillations that continue throughout both systole and diastole, and which are caused by the fibrillary contractions of the atria. These fibrillary waves have been divided into three classes: (1) *fine fibrillation*, where the waves are extremely rapid and minute; (2) *coarse fibrillation*, in which the oscillations are larger, though quite irregular in form and size and (3) *atrial flutter*, characterized by rather large uniform undulations and a regular rhythm. This last form deserves separate consideration (See below). The pulse rate in patients with atrial fibrillation varies usually between 80 and 150.

The condition may occur at any age, and is much more common in males than in females. It is always associated with serious lesions of the myocardium. It is very often associated with valvular lesions, and when it occurs in women, it is most often associated with mitral stenosis; as Thomas Lewis puts it, "mitral stenosis and auricular fibrillation are bosom companions." In about half the cases, a history of rheumatic fever is obtainable. Of the non-rheumatic cases, other infections, especially lues and influenza, are common antecedents; but atrial fibrillation may develop in any one of several different forms of myocardial degeneration; I have met with several instances in the thyreotoxic heart.

Patients with atrial fibrillation nearly always show signs, and complain of the symptoms, of cardiac decompensation with chronic circulatory insufficiency (*q. v.*).

The occurrence of atrial fibrillation in mitral lesions is often the cause of diagnostic blunders. As T. Lewis has pointed out, a murmur of mitral stenosis that originally extends through the whole diastole of the shorter cycles, "is replaced, as the heart slows, by an early diastolic murmur that is maximal in the region of the apex. It is the last murmur that so frequently misleads the physician and suggests to him an insufficiency of the aortic valves." When mitral stenosis and atrial fibrillation "are present in the same patient *and the heart rate is slow*, an early diastolic murmur most clearly audible at the apex but often spreading beyond it, is an expected sign. A diagnosis of aortic reflux is never justifiable when the heart is grossly irregular and slow, unless unequivocal signs of it are present apart from such a murmur."

It is in cases of atrial fibrillation that drugs of the digitalis group yield their most brilliant benefits. A heart rate above 100 in
is an indication for digitalis, or strophanthin, in amounts
the rate to 80 or lower. Patients with atrial fibrillati
tachycardia who do not respond to rest and to digitalis
tered are in grave danger.

When the atria once begin to fibrillate, the conditio
manent (*perpetual arhythmia*). But cases of *paroxys*

known and are often confused with simple paroxysmal tachycardia. The electrocardiogram quickly differentiates between the two conditions.

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(*d*) *Atrial (or Auricular) Flutter*

In this condition, the normal beats of the heart disappear and are replaced by heart beats originating in the atria as a result of automatic, regular, recurring pathological impulses, which vary in rate from 200 to 350 per minute.

The condition differs from simple paroxysmal tachycardia (1) in that the atrial rate exceeds 200 per minute, ordinarily being from 260-320 per minute, and (2) in that the ventricular rate is usually from 130-160 per minute, or exactly half the atrial rate, owing to the existence of a 2:1 heart block. Occasionally, the ventricular rate is much less, owing to the existence of a 3:1 or a 4:1 heart block, or there may even be ventricular bradycardia with a pulse rate of 30-38 per minute, owing to complete heart-block.

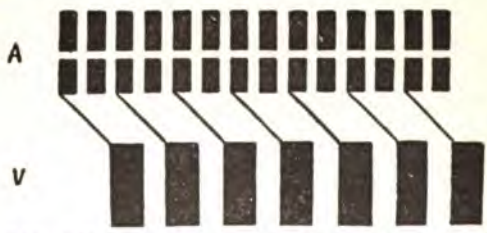

Fig. 260.—Diagram of Atrial and Ventricular Beats in Atrial (or Auricular) Flutter. The Abnormal Atrial Beats are Broken in their Centers. The Atrial Rate is Very Rapid. The Ventricular Rate, though Rapid, is only Half the Atrial, since a 2:1 Heart Block Exists. (After T. Lewis, "Clinical Disorders of the Heart Beat," published by P. Hoeber, New York.)

It is believed that, in atrial flutter, the pathological stimuli arise at a single focus in the atrial tissue, and that this focus lies at some distance at least from the pacemaker of the heart and is ungoverned by the cardio-inhibitory nerves.

Flutter is most common in advanced life (age 50-80), but i
as early as the third decade. Males are much more often a
females.

It is not always easy to recognize the condition clinically
trocardiographic studies, though sometimes it is possible. It
pected in elderly patients who have a regular pulse and pe

cardia of from 130-160 per minute, especially if there be no change of rate on change of posture, on rest, or on exercise. If electrocardiograms be taken in such patients, the atrial rate will usually be found to be just twice the ventricular rate; in other words, the condition is, as a rule, associated with 2:1 heart block.

But, in some patients with atrial flutter, the ventricular responses may be irregular, though, on exercise, the ventricular action becomes accelerated and perfect regularity of the pulse may then follow (T. Lewis). When flutter exists with a heart rate within normal limits, and with a regular pulse at the wrist, it is almost sure to be overlooked unless an electrocardiogram be made. Fortunately, in such cases, failure to detect the flutter is relatively unimportant; moreover, such cases are rare.

Many patients have short paroxysms of atrial flutter, resembling paroxysms of simple paroxysmal tachycardia; they may occur off and on for a considerable period before persistent flutter sets in.

It is remarkable how little subjective disturbance atrial flutter may cause. The patients complain, it is true, of fatigability and of a feeling of exhaustion, but otherwise they may be completely free from subjective disturbances. Now and then, the heart block, usually present in flutter, passes off; the ventricular rate then becomes immediately doubled so as to assume the full atrial rate of say 300 per minute. In such an attack, the patient often becomes unconscious, and, unless the heart block returns, he may soon die. Thomas Lewis has known flutter to last for four years in one patient whose ventricle beat unceasingly at the rate of 160 per minute. He states that of 17 patients manifesting flutter observed by him, only one has died and he as a result of operation.

It is interesting that the ventricular rate in flutter can be reduced by full doses of digitalis or of strophanthin. Sometimes the flutter ceases under such medication to be replaced by atrial fibrillation, after which, if the treatment with digitalis be stopped, the fibrillation may vanish and a normal rhythm be resumed!

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6. Changes in the Contractile Force of the Heart

(a) *Pulsus alternans*

The contractile force of the ventricular muscle may be diminished either from weakening of the muscle itself, or from the fact that the heart rate may be so rapid (*e. g.*, in some cases of paroxysmal tachycardia) that

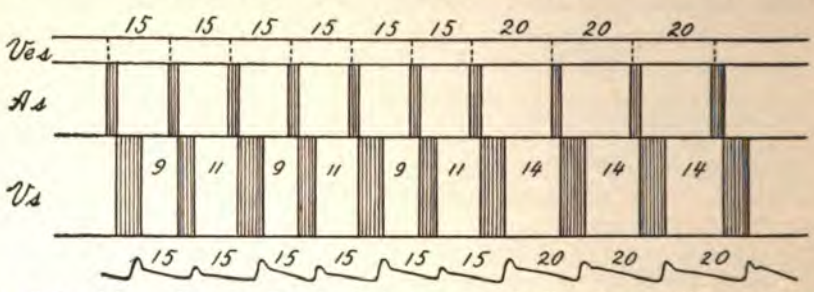

Fig. 261.—Pulsus alternans Due to Disturbance of Cardiac Contractility. (After K. F. Wenckebach, "Arch. des maladies du cœur," published by Baillière et Fils, Paris.)

there is not sufficient time in diastole for its recuperation. This is often evidenced by a rhythmic variation in the strength of alternate contractions of the ventricle. The heart beats regularly, but larger and smaller quantities of blood are expelled at alternate contractions.

Pulse Tracings (Fig. 262).—It is best seen in arteriograms from either the carotid or the radial arteries. The alternating large and small pulse waves indicate the variation in the forces of the ventricular contraction.

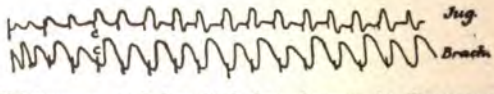

Fig. 262.—Jugular Phlebogram and Brachial Arteriogram in Paroxysmal Tachycardia with Ventricular Venous Pulse. (After A. D. Hirschfelder, J. H. H. Bull.)

In arteriograms of pulsus alternans the beats, though unequal in size, are seen to occur at approximately equal intervals; whereas, in beats resulting from regularly recurring premature contractio *bigeminus*), the pause following the premature contraction lengthened.

Electrocardiogram.—This, in many instances, is uncha sionally a similar variation in the height of the waves may in the cases reported, a peculiar feature is that the larger

tions correspond to the beats that produce the smaller arterial pulsations; in other words, excitation may be greater when contraction is less!

Significance.—Alternation of the pulse is a sign either that a fairly healthy heart is overloaded, or that a diseased or intoxicated heart muscle is making the effort to do more work than it is equal to.

In some instances, the alternation of the pulse is distinctly perceptible to the palpating finger; but, in the majority, graphic methods of registration are necessary for its recognition. It should be tested for by sphygmography in cases of angina pectoris and in all cases of high blood pressure (cardiac disease, arteriolar nephropathy), especially in elderly people. When extrasystoles are present, alternation should be looked for in the beats that immediately succeed them. Persistent pulsus alternans is a sign of bad omen and demands careful protection of the heart.

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7. Disturbances in Conduction in the Heart (Heart Block)

The different chambers of the heart are connected, as we have seen, through a distinct, specialized structure, by means of which the stimulus is passed from one to the other. This is the atrioventricular bundle of His, which begins in the atria and from them passes down to the ventricular septum, where it divides, in a Y-shaped manner, into two limbs, one going to

the muscular wall of the right, the other to the muscular wall of the left, ventricle. Each limb of the bundle is distributed by means of the Purkinje system of fibers in the ventricular wall. Functional or organic changes in the bundle may delay, or prevent, the transmission of the stimulus to the succeeding portion of the heart. When this defect does occur, it gives rise to a disturbance of the cardiac cycle, characterized by a partial, or a complete, dissociation of the contractions of the two parts of the heart separated by the lesion. To this condition of dissociation, the term **heart block** has been applied. The most common form is that in which block develops between the atria and the ventricles; and this is the type that is sometimes accompanied by the clinical picture of the **Adams-Stokes syndrome.** The obstruction may, however, affect other points in the conducting system. Recently, it has been shown that one branch of the bundle after its division may, alone, be affected, giving rise to an *intraventricular block.* Heart block is divided into classes primarily according to the location of the lesion, but these groups may be again subdivided, according to the degree of the disturbance produced. We meet with different grades of severity, which have been termed: (1) delayed conduction, (2) partial heart block; (3) complete heart block. In each of these forms, again, slightly different pictures may be encountered, both clinically and in the curves obtained by graphic registration.

(*a*) *Atrioventricular Block*

i. Delayed Conduction

When conduction is slightly impaired at the atrioventricular junction, the stimulus from the atria reaches the ventricles, it is true, but more time is required for its transmission than in normal conditions. This is spoken of as *delayed* conduction, and is usually the first stage of a beginning block. It is manifested in the heart by the increase in the time between the atrial systole and the ventricular systole (A

Fig. 263.—Delayed Conduction. Increase of As-Vs Interval. (A) A Diagram Representing the Action of the Normal Heart. The Auricle Contracts First and Transmits an Impulse (the Oblique Line) to the Ventricle. The Ventricle Responds and Commences to Contract Immediately at the Cessation of Auricular Systole; (B) A Diagram Illustrating the Earliest Stage of Heart Block. There is Delay in the Transmission of the Impulse from Auricle to Ventricle (Indicated by the Obliquity of the Line that Joins the Rectangles in the Diagram). (After T. Lewis, "Clinical Disorders of the Heart Beat," published by P. B. Hoeber, New York.)

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space separating the atrial from the ventricular waves, that is, in the lengthening of the *As-Vs* interval. In the venous tracing, this is the *a-c* interval, while in the electrocardiogram it is the *P-R* (*or P-Q*) interval, *i. e.*, what is now called the "alpha interval." This interval in normal hearts ranges from 0.1 to 0.2 of a second in duration, but in delayed conduction it may be increased to as much as 0.6 of a second. The longest

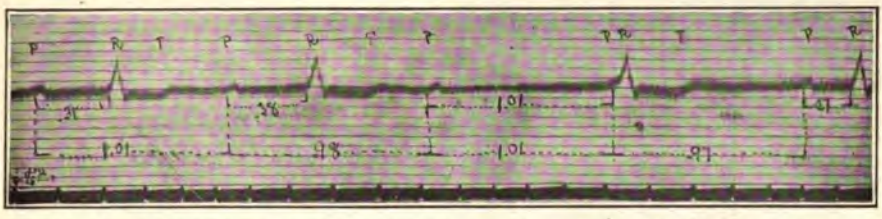

Fig. 264.—Remarkable Delay in Conduction Time with Beginning Heart Block. Personal Observation. Note that the *P-P* Interval Varies Between .97 and 1.01 Second. The *P-R* Interval for the First Cycle is .31, for the Second Cycle .38, for the Third Cycle the Extraordinary Length of 1.01 Second, so that the Ventricular Complex is Practically Coincident with the *P*-Wave of the Next Cycle. This Last *P*-Wave is Not Followed by a Ventricular Complex. The Final *P*-Wave in the Tracing is Followed by a Ventricular Complex After Leaving an Interval of .27 Second. The Rhythm Here is Thus 5:4, Since One Ventricular Complex Falls Out. (Electrocardiogram by Dr. E. W. Bridgman.)

interval recorded hitherto occurred in a case reported by my colleague, Professor W. S. Thayer. A still longer delay in conduction-time is observable in a patient now under my observation, referred to me for study through the kindness of Dr. McCurdy of Frederick, Md. The *P-R* interval in one cardiac cycle reached the great length of 1.03 second, as was shown by the electrocardiogram made for me by Dr. Bridgman. In the accompanying figure, an alpha interval of 1.01 second is shown.

ii. Partial Block

When the lesion is more advanced, conduction may be so impaired that the stimulus from the atria is occasionally prevented from reaching the ventricles; this is known as *partial block*. In the heart itself, it is manifested by failure of the ventricles to contract after certain contractions of the atria or auricles; in other words, certain beats are "dropped." There may be only an occasional dropping of a beat, or the atrial rhythm may have a definite ratio to that of the ventricles. Thus we speak of a 2:1, a 3:1, and a 4:1 block, these figures indicating the ratio between the numbers of the atrial and the ventricular contractions. Very often, as a

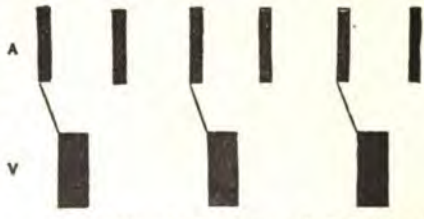

Fig. 265.—A Diagram of 2:1 Heart Block in which Alternate Ventricular Beats are "Dropped," though the Atrial Beats are Regular. (After T. Lewis, "Clinical Disorders of the Heart Beat," published by P. B. Hoeber, New York.)

This condition has been called *complete dissociation* or *complete heart block.*

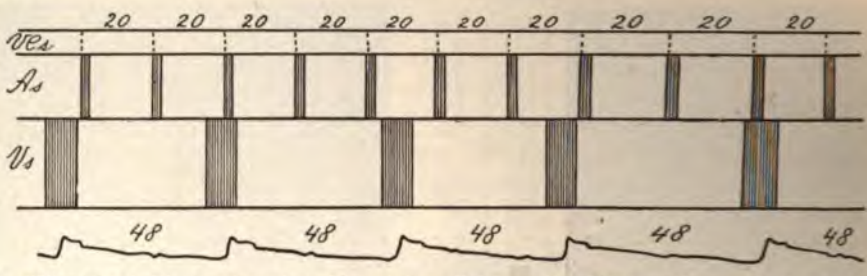

Fig. 269.—Heart Block. Complete Dissociation Betwe the Contractions of the Auricles and Those of the Ventricles. (After K. F. Wenckebach, "Arch. des maladies du cœur," published by Baillière et Fils, Paris.)

Pulse Tracings (Fig. 270).—The arteriogram in total block shows a series of very slow, forcible pulsations coincident with the ventricular rhythm; the pulse waves are separated by long diastolic pauses. A simultaneous jugular tracing shows *c*- and *v*-waves synchronous with each pulsation on the arteriogram, but in addition there are many small waves (scattered at regular intervals throughout the curve), which represent the

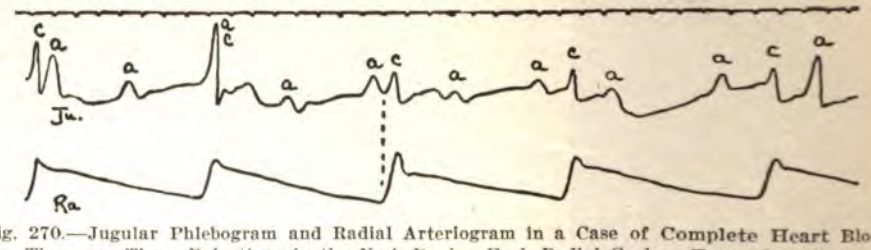

Fig. 270.—Jugular Phlebogram and Radial Arteriogram in a Case of Complete Heart Block. There are Three Pulsations in the Neck During Each Radial Cycle. Two of Each Group of Three Neck Waves Result from Atrial (or Auricular) Contractions, *a*, while the Third is the Result of Ventricular Systole, *c*; when *a* and *c* Fall Together an Exaggerated Wave is Produced and is Visible as such in the Neck; it is Due to Discharge of the Atrial Contents into the Veins. (After T. Lewis, "Clinical Disorders of the Heart Beat," published by P. B. Hoeber, New York.)

a-waves of the atrial rhythm. In differentiating total block from partial block, the main point to note is the complete independence of the two rhythms—atrial and ventricular—in the former condition. While there may be places where an *a*-wave and a *c*-wave seem to be associated in the usual relation, if the tracing be examined through a nu
will be seen that this relationship does not recur with any

Electrocardiograms (Fig. 271).—The features of the t
be much more readily demonstrated in electrocardiograms.
lar systoles, occurring as a regular rhythm, are marked by
T-waves of the normal form of ventricular complex. This i
the ventricular rhythm is not due to contractions of extra

and that the inherent rhythm of the ventricles originates well up in the ventricular conduction-system. The rhythm of the atria, as evidenced by

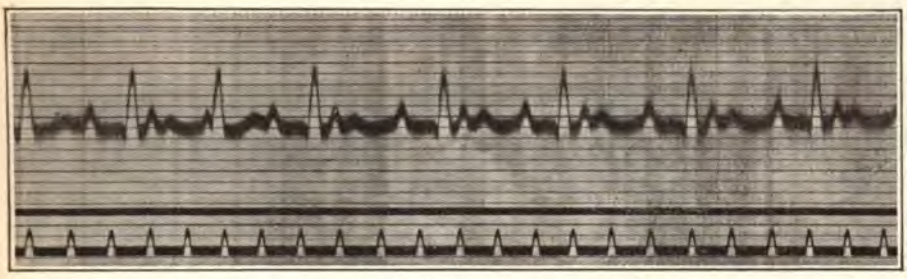

Fig. 271.—Electrocardiogram in Complete Heart Block. The Ventricular Rhythm is Shown by the High, Sharp *R*-Waves. The Smaller Atrial or Auricular Waves, *P*, can be Seen at Regular Intervals on the Curve. The Two Rhythms are Absolutely Independent of One Another. The *T*-Waves are Easily Distinguishable from the *P*-Waves.

the *P*-waves, seems to be superimposed upon, but completely dissociated from, the ventricular rhythm.

(*b*) *Intraventricular Block*

Normally, the right and left ventricles are stimulated simultaneously through the two branches of the atrioventricular bundle of His, but, in some instances, the path of conduction to either the right or the left side may be obstructed, in which event, the stimulus passes to one ventricle only and is thence transmitted through the muscular wall of the heart to the other ventricle. This muscular connection between the two ventricles is, however, so intimate that no asynchronism of the ventricles can be demonstrated by clinical observation of the heart itself or by any of the simpler mechanical methods of registration. It is only by means of a study of the electrical variations that we become aware of this change in the form of the ventricular contraction.

Electrocardiograms (Fig. 272).—The curve in intraventricular block shows a regular rhythm, each cycle of which is made up of an atrial *P*-wave, followed, after the usual interval, by a ventricular wave. This indicates that, in every instance, the ventricular contraction is the result of a stimulus conducted from the atrium after the preceding atrial systole. The ventricular part of the curve, however, does not exhibit the features of normal supraventricular stimulation, but is of the form produced in heterogenetic beats, or extrasystoles, of the ventricle. The diphasic wave of an extrasystole of ventricular origin is explained by the fact that a heterogenetic beat arises in the wall of one ventricle and is thence transmitted to the wall of the other. The same principle, it is believed, holds good for the curve seen in intraventricular block, the stimulus from the atrium being able to reach one ventricle directly and not the other owing to the

existence of an obstructive lesion in one branch of the bundle of His. We have seen that we can decide, by a study of the form of the electrical curve in a ventricular extrasystole, which ventricle is first stimulated; in intraventricular block we can also, from a study of the electrocardiogram,

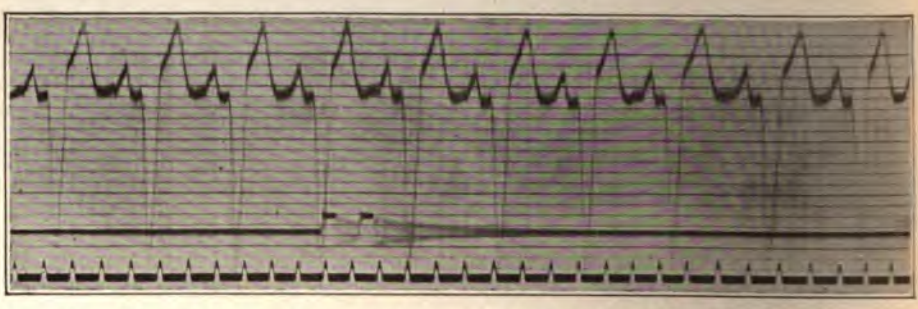

Fig. 272.—Electrocardiogram from a Patient with a Lesion of One Branch of the Bundle of His. This Peculiar Form of Electrocardiogram is Observable in Partial Lesions of the Bundle of His. The Atria (or Auricles) Contract in the Usual Manner as Shown by the Normal Form of *P*-Wave. Each Atrial Wave, however, is Followed by the Ventricular Complex that is Usually Associated with a Ventricular Extrasystole. This Indicates that though the Ventricles Receive the Impulse from Above, One Ventricle Contracts Before the Other, as in an Extrasystole. This Phenomenon is Explicable by Assuming a Lesion of the Bundle of such a Sort that the Stimulus to One Side is Blocked, though that to the Other is Not. In the Curve Above, the Block is in the Right Ventricle and the Left Ventricle Contracts First. (Heart Station, J. H. H.)

make out which ventricle contracted first, and thus locate the lesion that causes the block in the branch of the bundle on the opposite side.

Etiology of Heart Block.—Heart block may be due either to functional disturbance (reflex vagus inhibition, overdose of digitalis or strophanthin), or to organic changes in the His bundle (fatty degeneration, fibrosis, gumma, atherosclerosis, calcification, tumor, anemic necrosis from thrombosis, or acute inflammatory infiltrations). In cases that have come to autopsy, the lesion has most often been found either in the Aschoff-Tawara node, or in the main trunk of the bundle.

In 1909, Hirschfelder and I reported experiments in which we were able in animals to cut one branch of the bundle (Fig. 273).

The Adams-Stokes Syndrome.—For decades it has been known that patients with marked bradycardia are subject to characteristic attacks of fainting, arrested respiration, and epileptiform convulsions. The syndrome was described in 1827 by Adams, and, later on, also, by Stokes. In 1897, His observed the syndrome, and found by studies of the venous and arterial pulse that, in the bradycardia, the atria and the ventricles were contracting at different rates, and that many atrial contractions occurred without any corresponding ventricular contractions. His gave the name "Heart Block" to this condition. Block in animals had been known before to the physiologists Gaskell (1883) and Engelmann. The whole subject was later on illuminated by the brilliant experimental researches

of Erlanger, who, in Howell's laboratory, devised an ingenious method by which all forms of conduction disturbance, from delay, through partial block, to total block, could be produced experimentally. It seems probable that when the typical syncopal attacks occur in human beings there is a sudden change from partial to total block.

A syncopal attack may be very transient; as a rule, it lasts 5 to 10

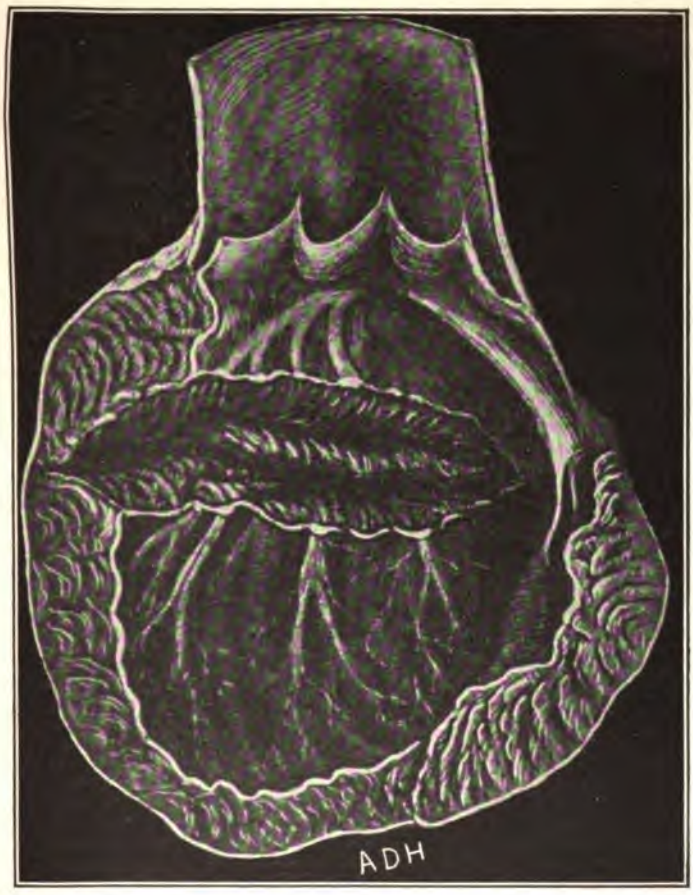

Fig. 273.—Wall of the Left Ventricle, Showing a Cut Through All the Ramifications of the Left Branch of the Atrioventricular Bundle, which Appear Lighter than the Rest of the Heart Muscle. (After L. F. Barker and A. D. Hirschfelder, Arch. Int. Med.)

seconds. Attacks are prone to occur in groups. A patient may be free from attacks for months or years, then have a period of a few days or weeks in which single attacks or groups of attacks occur, to be followed again by a free period. The number of attacks varies much. Some patients have only a single attack in a month; some have 20 attacks per day; and His has reported a case in which a patient had 143 attacks within

twenty-four hours. The pulse is usually 28-34 at the time of attacks; but as low a rate as 8-17 per minute has been observed.

Diagnosis of Heart Block.—The condition may be suspected clinically when there are "dropped beats," or when there is a permanent bradycardia of high grade, or if the patient gives a history of syncopal attacks. But, to make an accurate diagnosis, graphic methods are essential. Electrocardiograms are the most satisfactory, but if they are unobtainable, the condition can be analyzed, with the use of the polygraph, in simultaneously-recorded phlebograms and arteriograms (see above).

In addition to the accurate information afforded by graphic methods, certain clinical features are worthy of attention. In *delayed conduction*, if the *As-Vs* intervals be long, the sounds of the atrial contractions may be audible, separate from those of the ventricular contractions; when a "reduplicated first sound" is audible, or when a "double second sound" can be heard, the possibility of delayed conduction should be kept in mind.

In cases where *single beats are "dropped,"* the phenomenon may be due either to a silence of the whole heart (sinus irregularity) or to a ventricular silence after an atrial contraction; in the latter instance, the dropped beat is not regularly associated with a definite respiratory phase.

In *2:1 heart block*, the ventricular rate is usually between 40 and 50 per minute. When this occurs in mitral stenosis, there may be two thrills and two diastolic murmurs (due to atrial contraction) for each single ventricular cycle (T. Lewis).

In *complete heart block*, the pulse rate is often quite regular at a rate of 28-34 per minute. Listening over the heart, a first and a second sound are audible for each ventricular beat, but on listening attentively, faint muffled sounds, due to atrial systoles, may be heard in the long diastoles. Moreover, waves synchronous with the atrial systoles may be visible in the jugular veins.

It should, of course, be emphasized that heart block and the Adams-Stokes' syndrome are not synonymous terms; "the majority of patients who exhibit heart block never have fits" (T. Lewis). I have observed one patient who has had complete heart block for years without syncopal attacks; in addition to his regular ventricular automatic rhythm, he has many ventricular extrasystoles.

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B. Circulatory Insufficiency

The circulation may become insufficient, either through failure of the motor (myocardial insufficiency) or through failure of contraction of the peripheral arterioles (vasomotor paralysis).

In *myocardial insufficiency,* the reserve force of the heart is the first to suffer; the heart may do its work fairly well when the body is at rest, but it is unable to meet the extra demands for work that muscular effort throws upon it. It loses its "power of accommodation."

Myocardial insufficiency is usually responsible for **chronic insufficiency of the circulation.**

In acute infectious diseases, *vasomotor paralysis* is most often the cause of the **acute insufficiency of the circulation** that sometimes develops; it was formerly believed to be due to "heart failure." An acute insufficiency of the circulation may, however, occasionally be due to *acute dilatation of the heart* from myocardial injury following overexertion or intoxications.

In order that the blood pressure may be kept sufficiently high, two factors are necessary: (1) a sufficient amount of blood must be expelled into the aorta, the **minute-volume** here depending upon (a) the systolic output and (b) the frequency of ventricular contraction; and (2) a sufficient **peripheral resistance** must be maintained through contraction of the arterial musculature under the influence of the vasomotor nerves.

In the processes of "compensation," therefore, delicate adjustments have to be made between the minute-volume on the one hand and the peripheral resistance on the other. In a given case of circulatory insufficiency, it may be very difficult to decide in how far each of the several factors concerned in the maintenance of the circulation under normal circumstances may be involved. Now that we have begun to realize, through the researches of K. Hasebroek and others, the active part played by the muscle of the arteries, not only in the regulation of the peripheral resistance and the distribution of the blood, but also in supplying a part of the driving energy of the circulation, the difficulty increases.

1. Chronic Circulatory Insufficiency

Definition.—This is a condition in which the power of accommodation of the heart is impaired or lost; in the milder cases, the reserve force of the heart is lessened; in the severer cases, the heart is unequal to the tasks

thrown upon it even when the patient is completely at rest—the state of "decompensation" exists.

Etiology.—The causes of chronic circulatory insufficiency lie either in the heart itself (organic diseases of this organ, especially of the myocardium), or in disturbances of the heart secondary to diseases elsewhere in the body (*e. g.*, atherosclerosis, chronic nephropathies, thyreointoxications, pulmonary emphysema).

The varied causes of chronic circulatory insufficiency may well be considered in relation to their effect upon the heart. To one class of etiological factors the heart shows little or slight adaptative reaction; myocardial insufficiency is primary and myocardial hypertrophy is absent or but imperfectly developed. In a second type of case, however, the stage of circulatory insufficiency is preceded by a period in which, by hypertrophy, the heart has remained competent in the presence of conditions that increased its work above normal limits.

To the *first class* belong those cases in which progressive circulatory insufficiency develops as a result of some toxic action, as in hyperthyroidism, or in infectious diseases such as typhoid fever. Here also should be classed the gradually developing circulatory insufficiency seen in acute endocarditis, and in acute myocarditis. The more active cases of luetic aortic insufficiency show this same tendency to progressive myocardial failure, the compensatory hypertrophy being unable to keep pace with the development of the valvular lesion. In the so-called "fatty heart," and in the senile fibroses of the myocardium, a slower, but similarly unchecked, march of events takes place.

In certain of the above cases the heart may recover upon the disappearance of the cause of myocardial failure. Apparently, normal function may be regained, or a chronic valvular or myocardial lesion may remain against which the heart protects itself by adaptative reactions.

The *second class* of causes of circulatory insufficiency includes those whose nature is such as to place an extra burden of work upon the heart. Insufficiencies and stenoses of the cardiac valves; pericardial adhesions; hypertension of nephritic or atherosclerotic origin; increased resistance in the pulmonary circulation due to fibrosis of the lungs or to emphysema; increase in the volume of blood, plethora vera. At first, in all these cases, the extra demands made upon the heart are met by hypertrophy of one or both sides of the organ, but as increasing age tends to multiply these burdens, the reserve power of the heart becomes ever smaller.

Symptoms.—These vary greatly in single cases, for reasons which we do not as yet know. The stasis in the several organs varies, and the resistance to stasis by the organs seems also to be an individual affair.

Of the SUBJECTIVE SYMPTOMS complained of, dyspnea, distress in the region of the heart or liver, digestive disturbances, and abnormal feelings in the head are most common. Cough is a very common

Dyspnea is the most constant symptom, being noticed
tion. In severer cases, paroxysmal attacks of dyspnea—the
diac asthma"—may be very disturbing; they point to a f
tricle, and, sometimes, herald the onset of pulmonary edema

Distress in the region of the heart may cause consid
It seems to be due either to dilatation of the ventricles

the cardiac muscle, either of which can give rise to "referred pain." Outspoken stenocardiac attacks, or angina pectoris, point to sclerosis of the coronary vessels.

Pain, or soreness, in the right hypochondrium is probably due to the stretching of Glisson's capsule, as the liver enlarges, owing to chronic passive congestion.

The digestive disturbances are doubtless due chiefly to stasis in the venous system. They include anorexia, bloating after eating, and constipation. Vomiting and diarrhea are frequently present.

Abnormal feelings in the head include headaches and dizziness. Many patients complain that they cannot concentrate their minds properly and that they feel depressed.

Of the OBJECTIVE FINDINGS, may be mentioned (1) changes in the heart itself and (2) stasis phenomena elsewhere in the body.

In the heart, the signs of *hypertrophy*, of *dilatation*, or of both are present (*q. v.*). These are easily made out by physical methods and by x-ray examinations. Changes in pulse rate are nearly always met with and arhythmia is common. In many cases, evidences of valvular lesion are present.

Of the *stasis phenomena*, the commonest are edema, oliguria (with albuminuria and cylindruria), cyanosis (with tachypnea and dyspnea), and palpable enlargement of the liver and, sometimes, of the spleen. Soon, or later, signs of edema of the lungs appear, and we can make out dullness at the bases, râles, and diminution of the breath sounds. The sputum contains "heart-failure cells."

The *edema* of cardiac decompensation shows the effects of gravity, being most marked in dependent parts. Patients that are up and about show it, first, at the ankles, about the malleoli; those that lie in bed may manifest it over the sacrum or in the backs of the thighs. Sometimes the scrotum is very edematous. In contrast with edema of renal origin, the face is less affected than the extremities. As the circulatory insufficiency develops, general anasarca may appear, with dropsy of the serous cavities. Sometimes, a hydrothorax or an ascites may precede the subcutaneous edema.

The oliguria is one sign of a *stasis nephropathy;* other urinary changes include a high color and high specific gravity and the presence of albumin and casts. Formerly there was difficulty in distinguishing such a stasis nephropathy secondary to chronic circulatory insufficiency from other nephropathies, but with the use of the renal test diet (*q. v.*) and of functional tests, differentiation is easier.

Cyanosis of the lips, cheeks, and other acra (fingers, toes) is often present. It is due to venous stasis, and is often associated with polycythemia rubra (*q. v.*) and increased viscosity of the blood. The respiratory rate is increased (tachypnea) and the respirations are labored (dyspnea);

often the patient is compelled to sit up in bed, or to be propped up, through the night, a condition known as orthopnea. In such cases, besides lung-stasis, the possibility of hydrothorax should be kept in mind. Cheyne-Stokes' breathing is not uncommon. Acute edema of the lungs is rarely seen in chronic myocardial insufficiency except as a terminal phenomenon.

The swelling of the liver, due to chronic passive congestion, often becomes demonstrable, by palpation, early. The lower edge may be felt below the costal margin, the consistence is firm, and the organ is tender. In advanced cases, the liver edge may be as low as the umbilicus. The enlargement of the liver may also extend upward, dislocating the diaphragm (percussion, röntgenoscopy). Occasionally, there is slight icterus. The spleen may, or may not, be palpable.

The actual *onset* of the chronic circulatory insufficiency may be gradual, or it may follow as a direct sequel of an acute decompensation of the heart due to sudden demands in excess of its reserve power. In either case, if the causal condition is not of a rapidly progressive nature, or if the damage done is not already too extensive, the freeing of the heart from all unnecessary work may allow it to become competent again, temporarily. Chronic circulatory insufficiency, in these cases, is, characteristically, a disease of remissions.

Patients in whom the onset is gradual often present, over a long period of time, the clinical picture of a MILDER GRADE OF RELATIVE CARDIAC INSUFFICIENCY. Such patients notice *shortness of breath* on slight exertion, or after eating a heavy meal. They may wake suddenly at night with a choking sensation, which passes off when they sit up. A chronic *cough* often develops; this may occur in paroxysms. A feeling of oppression, or even of *pain,* in the cardiac region is frequently noted. Sudden exertion, or change in position, causes marked *dizziness.* Sooner or later the patients usually discover the presence of some *edema* about the ankles, appearing toward the end of the day. In appearance, they are often slightly *cyanotic.* Traces of breathlessness may show in their speech, and a nervous manner is not uncommon. The findings upon examination of the *heart* will depend upon the condition responsible for the myocardial insufficiency. Hypertrophy may or may not be present, but a moderate dilatation of one side of the heart is a frequent finding. Evidence of organic valvular lesions may be present. A relative insufficiency of the mitral valve is common. The rhythm may be regular but it is more usual to find some extrasystolic arhythmia, or a gallop-rhythm at the apex (especially in nephritic hearts). Some degree of tachycardia is the rule. The *blood pressure* will depend largely upon the condition to which the cardiac signs are primarily due. At the base of the *lungs,* posteriorly, a slight impairment of the percussion note may be found, along with a few moist râles. A palpable, *tender liver-margin,* when present, is a valuable confirmatory sign. A trace of albumin and occasional casts in the *urine* are to be expected as a result of renal stasis. The *edema* of the lower extremities may be very slight or absent. It should be carefully looked for; it is often earliest discovered over the lower
or behind the malleoli. It may be more marked on the left leg.
the tissue on pressure is characteristic.

The clinical picture of COMPLETE CARDIAC DECOMPENSATION is a
ing one. The *dyspnea* reaches higher grades; the patient must re-
in the sitting position (*orthopnea*); during the frequent pseudo-a
the accessory respiratory muscles are all brought into play, t
the countenance is livid, the extremities cold, and cold perspirati

forehead. There is often Cheyne-Stokes respiration. Cough is frequent and exhausting. The *edema* is usually very marked. The legs, the external genitalia, the abdominal wall, and the lower back, are greatly swollen. The hands and arms may be likewise involved. The face is often spared, but infra-orbital edema and chemosis are common. The edema shifts, with changes of position of the patient, to the dependent parts. In cases of long standing, a distinct *icteric color* of the skin and conjunctivae is often present. *Cyanosis* is variable in degree. A marked *pallor* characterizes many cases. The *heart* is dilated; the apex impulse is diffuse and wavy; the right and left cardiac borders are displaced lateralward. The heart sounds are blurred and softened. If murmurs of organic valvular disease were previously present, they have usually grown much fainter, or have disappeared. Blowing murmurs of relative mitral and tricuspid insufficiency may be detected. Marked disturbances in the cardiac rhythm are the rule; of these the most common are those due to auricular fibrillation or to extrasystoles. The heart rate is rapid and varies with changes in the patient's condition (100-140). The *pulse* is often difficult to count, since many beats do not reach the wrist ("pulse-deficit") and the volume is small. The *blood pressure* is usually lowered. There occur cases, however, in which a rise in blood pressure accompanies decompensation of the heart. This is, occasionally, strikingly evident in cases of aortic insufficiency of luetic origin, and in cases of hypertensive renal disease. Engorgement of veins in the neck, and the systolic venous wave, due to tricuspid insufficiency, may be observed.

Throughout the body, functional disturbances and physical signs appear, indicative of the effects of *passive congestion* upon the viscera. The bases of the *lungs* show impaired resonance, the breath sounds are diminished, and crackling râles are heard. The sputum may be tinged yellowish-brown. Right-sided, or bilateral, hydrothorax is common. In cases of long standing, infarcts of the lung, often of considerable extent, should be watched for; they may develop with outspoken symptoms and signs, or may be cryptic. Whenever, in such a case, obscure signs of consolidation, accompanied by pleural friction, appear over a lower lobe, infarction should be suspected. Terminal bronchopneumonias are common. *Hydropericardium* is more frequently present than detected. Only careful daily observation of the outline of cardiac dullness and of the intensity of the heart sounds enables the physician to appreciate the appearance of this complication. The enlarged *liver,* tender especially in the earlier stages, may extend below the level of the umbilicus. The surface is smooth. When the edge can be grasped and pulsation felt, the diagnosis of tricuspid insufficiency is certain. Pain, due to hepatic distention, is, in some cases, a very prominent symptom. The congestion of the walls of the stomach and small intestine gives rise to many *gastro-intestinal symptoms.* The commonest of these are anorexia and constipation. Belching and flatulence, meteorism, and persistent vomiting, may all occur. In extreme congestion, hemorrhage *per diapedesis* occurs in the intestine, and the stools contain macroscopic blood. An acute colitis is, not infrequently, a terminal infection. The abdominal cavity, in all severe cases of myocardial insufficiency with edema, contains an excess of peritoneal fluid; but it is often difficult to detect this fluid until the amount is very considerable. The *urine* is scanty (300-700 c.c.), usually high-colored and of high specific gravity. Albumin, hyaline and granular casts, and a few red blood-cells are found. In addition to the stasis-kidney, the presence of an underlying nephritis, should it exist, may be discoverable only by means of a careful study of the renal function (*q. v.*) and by the presence of the extrarenal features of this disease. *Psychical symptoms* are common in myocardial insufficiency, and may closely resemble those seen in uremia. Nocturnal delirium and restlessness may necessitate a close watch over the patient.

The *diagnosis* of chronic circulatory insufficiency should always be considered by the physician as only the first step in his attempt at a complete understanding of the case. Only after he has discovered the underlying cause of the myocardial failure will he be able to employ rational therapeutic measures, or to offer a logical opinion as to the prognosis.

Course of Myocardial Insufficiency.—All depends upon (1) the cause, and (2) the management. If the cause be removable, or if the injury to the heart muscle be relatively slight, brilliant results can be obtained from therapy. Even in the severer forms of myocardial insufficiency judicious management may achieve most gratifying results over a long period. Sudden death may, occasionally, occur from coronary disease, or, more rarely, from pulmonary edema. In slow cardiac death, the stasis phenomena increase, atrial fibrillation is common, and, at the end, a pneumonia, or some other infection, may supervene.

Diagnosis of Chronic Circulatory Insufficiency.—The existence of the insufficiency of the circulation is easily made out from the symptoms and signs described above. But the diagnosis of the underlying cause and of the exact pathological anatomy and physiology may be exceedingly difficult. Each case should be exhaustively studied by physical and graphic methods, and the study should not be confined to the circulatory organs but should include all the systems of the body.

In the *milder grades* (*relative insufficiency*), symptoms appear only on exertion, and the clews to diagnosis have to be gained largely from the anamnesis and from functional tests of capacity. In the *severer grades* (*absolute insufficiency*), the diagnosis "leaps to the eyes"; the dyspnea, the cyanosis, the edema, the abnormalities of the pulse, the changes in the heart, and the swollen, tender liver leave, as a rule, no room for doubt. In every case, besides confirming the signs of the circulatory insufficiency, an attempt should be made to explain its pathogenesis, in order that the therapy may be intelligently planned.

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2. Acute Circulatory Insufficiency

Definition.—A state in which there is a sudden development, within a few minutes or a few hours, of symptoms pointing to vasomotor paralysis, to acute myocardial insufficiency, or to both.

Etiology.—The commonest cause of acute circulatory insufficiency is intoxication of the vasomotor center, with vasomotor paralysis, in acute infectious processes (*e. g.*, in pneumonia, sepsis, typhoid). Sometimes, a sudden injury to the cardiac muscle may be responsible as in infections like diphtheria, in coronary embolism or thrombosis, or in violent overexertion (acute overstrain of the heart of athletes); in many of these cases, however, the heart muscle, supposedly healthy, has been the site, earlier, of a chronic inflammatory or degenerative process.

Symptoms.—These are exceedingly variable, depending upon the cause. In the rapidly developing VASOMOTOR PARALYSIS of acute infections, there is sudden collapse, the blood pressure (both maximal and [illegible] falls, the pulse becomes dicrotic, sometimes monocrotic, the [illegible] crated, and the vessel feels empty; the skin is pale, cool, and in cold sweat; the patient is prostrated, often delirious or co[illegible] heart's action may still be regular, and there is no overfilling [illegible] in marked contrast with myocardial insufficiency.

In ACUTE DILATATION OF THE HEART in acute infections, or

overexertion, the veins become overfull and the increase in the size of the heart can be made out by percussion and by röntgenoscopy. The right margin of the heart is often rapidly displaced to the right as the right ventricle dilates. Stasis phenomena quickly appear (crackles at the bases of the lung; swelling of the liver; scanty, high-colored, albuminous urine).

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C. Reparative and Adaptive Processes in the Heart

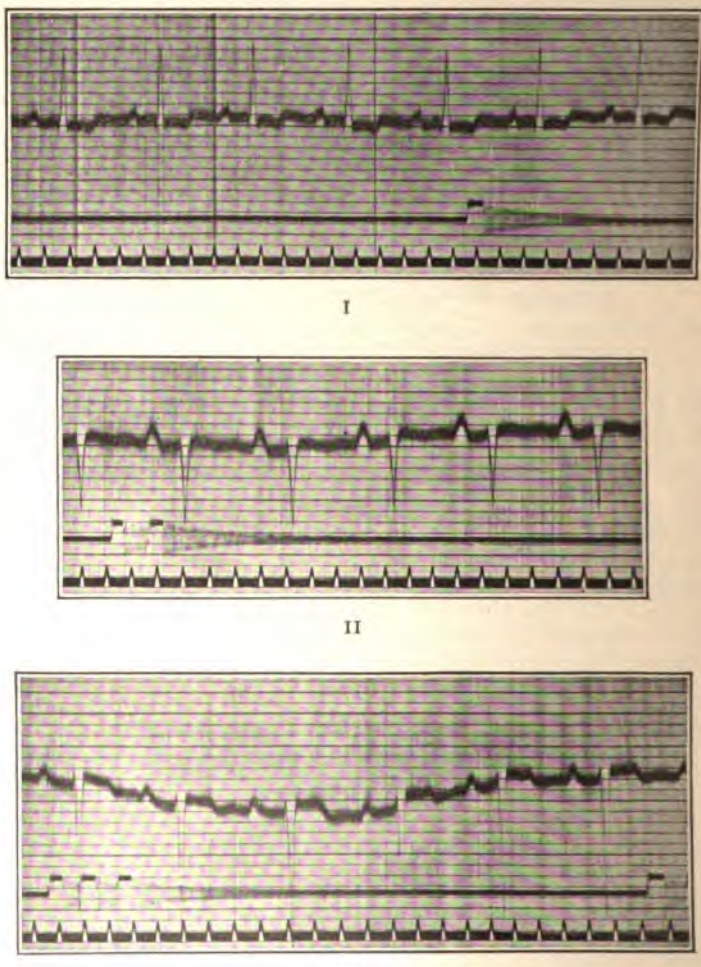
The heart muscle undergoes *hypertrophy* in adapting itself to increased work. The wall of the ventricle may become twice as thick as normal. The thickening is due to enlargement of the individual fibers, not to a multiplication of them. When the chambers of the heart undergo *dilatation*, this is due to the increased amount of blood that they are forced to contain. Dilatation is closely related to the *function of tonicity* of the heart muscle; it is, in some cases, a cardiac hypotony.

The heart, as a whole, may be enlarged from dilatation, from hype trophy, or from both; but, more often, one, or two, of its chambers will b found enlarged alone, or more than the other chambers.

1. Hypertrophies of the Heart

(*a*) *Hypertrophy of the Left Ventricle*

Physical Signs.—Here we see displacement of the apex beat downwar and lateralward. The impulse is stronger and more heaving than norma There is no marked change in the cardiac dullness unless there is dilatatio



I

II

III

Fig. 274.—Electrocardiograms in Hypertrophy of the Left Ventricle. Derivations I, II, and III Shown in Order. The Characteristic Feature, in this Condition, is the Inversion of the *R*-Wave, as One Goes from Derivation I to Derivations II and III.

as well as hypertrophy. Sooner or later, however, the dilatation accompanying the hypertrophy gives rise to an enlargement perceptible on percussion. On x-ray examination, the heart occupies a more horizontal position than normal, the third curve on the left side projects prominently, and the apex looks rounded and plump. The condition is often associated with arterial hypertension and with an accentuated aortic second sound. The electrocardiograms are characteristic.

Etiology.—The more important etiological factors include: (1) increased work due to valvular disease (most marked in aortic insufficiency and in aortic stenosis); (2) arterial hypertension in prolonged muscular overexertion (athlete's heart), in pregnancy, in nephritis, in some cases of arteriosclerosis, and in plethora vera; (3) sometimes "idiopathic" (no cause being ascertainable).

(*b*) *Hypertrophy of the Right Ventricle*

Physical Signs.—The apex beat is not more forcible than normal, but is rather diffuse, and is displaced to the left rather than downward. Rotary undulation is often visible in the precordium. The superficial and the deep areas of cardiac dullness are widened, especially to the right (due to accompanying dilatation). The pulmonary second sound is accentuated.

On x-ray examination, the "median position" of the heart is striking; and there may be noticeable projection of the lower of the two curves on the right, often due in part to accompanying dilatation of the right atrium. The pulse may be but little changed. The maximal blood pressure is often low.

Etiology.—This hypertrophy may be the result of various causes, including: (1) organic valvular disease, especially mitral disease, and (2) obstructions in the pulmonary system (stenosis of the pulmonary artery, emphysema, kyphoscoliosis, chronic bronchitis, arteriosclerosis of the pulmonary vessels). Hypertrophy and dilatation of the right ventricle accompany (3) insufficiency of the pulmonary valves and (4) tricuspid-valve lesions. In (5) congenital anomalies (patent ductus Botalli and patent foramen ovale), the right ventricle hypertrophies.

(*c*) *Atrial Hypertrophy*

The walls of the atria may also hypertrophy, in which case an exaggerated *a*-wave may be seen upon the jugular plebogram (right atrium), or upon the esophageal cardiogram (left atrium). The high *P*-wave in the electrocardiogram of mitral stenosis believed to be associated with atrial hypertrophy.

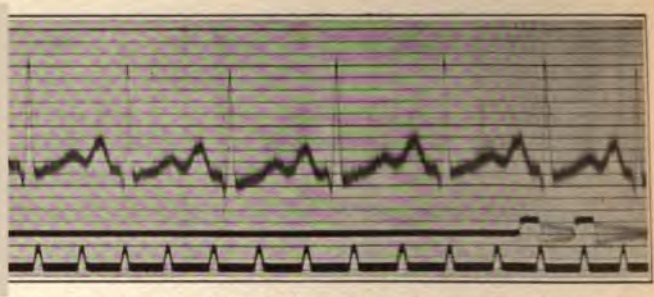


Fig. 275.—Electrocardiogram in Hypertrophy of the Atria (or Auricles). The Characteristic Feature of this Electrocardiogram is the Comparative Size and Height of the *P*-Wave. It is Almost Double that of the Normal *P*-Wave.

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2. Dilatation of the Heart (Failure of Tonicity)

The heart is limited in its power of adaptation by hypertrophy. Sooner or later, disturbances appear (decompensation due to myocardial insufficiency). When the left ventricle is weak, the blood will tend to be dammed back upon the lungs; when the right ventricle weakens, chronic passive congestion in the veins of the body sets in.

As the heart muscle weakens, the cavities surrounded by it dilate (dilatation of the heart from failure of tonicity). Hypertrophy of the heart, by itself, causes very little increase in the size of the heart demonstrable by physical methods; when the areas of cardiac dı
creased from enlargement of the heart, or when on x-ray e
larger volume than normal is visible, dilatation exists. T
cussion dullness and the fluoroscopic views (as orthodiagr
acteristic for dilatation of the single heart chambers (*q. v*
is common. The dilatation may involve all four cavities
usually, however, either the left heart or the right heart is
affected

Causes of Dilatation.—(a) In the HEART MUSCLE itself:

(1) From recurring inflammations in the heart muscle, especially those involving the conduction system; or

(2) From chronic intoxications (bacterial, alcohol, caffein, nicotin).

(3) From multiple infarctions (due to emboli, or to thrombosis);

(b) OUTSIDE THE HEART MUSCLE. The hypertrophic myocardium may fail on account of too great disproportion between the force of the heart and the resistance to be overcome. This disproportion may arise:

(1) At the cardiac orifices (from organic changes in the valves); or

(2) in the peripheral vascular system (general or pulmonary), from bodily overexertion, from infections, from arteriosclerosis, or from nephritis.

The real cause of dilatation, however, if there is not an actual leak back from the arteries, lies in overfilling of the heart from high venous pressure.

The symptoms are those of chronic circulatory insufficiency (*q. v.*).

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D. The Inflammatory Cardiopathies

These may be acute or chronic, and may involve the endocardium, the myocardium, or the pericardium. When all three are simultaneously involved, we speak of a *carditis* or of a *pan-carditis.*

1. Endocarditis

Definition.—An inflammation of the lining membrane of the heart.

Etiology.—In the majority of cases, if not in all, the cause lies in *bacterial infection,* though a toxemia may predispose to localization of

the bacteria on the endocardium. The bacteria get into the blood stream from some *primary focus of infection* (tonsils, teeth, paranasal sinuses, urethra, lung, etc.). Any one of several bacterial forms may set up an endocarditis. That most frequently responsible is the virus of acute rheumatic fever, the *Streptococcus rheumaticus;* but the *Streptococcus hemolyticus,* the *Pneumococcus,* the *Streptococcus viridans,* the *Gonococcus,* the *Staphylococcus aureus,* or the *Bacillus influenzae,* may be responsible. Less common agents are the meningococcus, the typhoid bacillus, and the colon bacillus. Endocarditis has been experimentally produced by injecting bacteria into the blood stream after mechanical injury to the heart valves.

Pathology.—Endocarditis may follow an acute, a subacute, or a chronic course. The left side of the heart is much more often involved than the right. The membrane over the valves is most often involved (*valvular endocarditis*); or the localization may be chiefly elsewhere, say on the chordae tendineae (*chordal endocarditis*), on on the walls of the atria or ventricle (*parietal,* or *mural, endocarditis*). The mitral valve is most frequently involved (60 per cent of the cases), the mitral and aortic together (30 per cent of the cases), aortic alone (3 per cent of the cases), tricuspid or pulmonary alone very rarely.

(*a*) *Acute Endocarditis*

Varieties.—Acute endocarditis may be classified on an etiological basis (rheumatic, gonococcal, etc.), or on a pathological-anatomical basis. The following main types are distinguishable:

(1) Simple Vegetative and Benign Endocarditis (*Thrombo-endocarditis superficialis, Endocarditis verrucosa, Endocarditis simplex*).—This is frequent as a complication of tonsillitis, rheumatism and other infectious diseases (chorea, scarlet fever, measles, gonorrhea, pneumonia, diphtheria). Numerous, minute, grayish-white deposits occur at the line of closure of the valves, on the chordae tendineae, or on the parietal endocardium; the warty deposits (or vegetations) are minute thrombi made up of blood platelets, white and red corpuscles and a little fibrin. The endothelium beneath them is dead; they lie on the subjacent connective tissue, which, proliferating, may later invade them; hence adhesions, thickenings, scarring and retractions develop and lead to chronic valvular diseases (stenosis, insufficiency) especially in recurring endocar

(2) Septic, Ulcerative, or Malignant Endocar
endocarditis septica, Endocarditis ulcerosa).—Here one
process, but the thrombi are larger and coarser and there i
destruction of valve tissue. Ulcers occur on the valves,
these at autopsy show many bacteria, usually cocci; th
especially on the septum over the left branch of the I

uncommon. Occasionally, a heart aneurism occurs and even perforation. Many bacteria (streptococci, pneumococci, staphylococci, gonococci) have been isolated during life in blood cultures from these cases. Septic emboli are formed, which cause infarction of the kidneys, spleen, heart muscle and brain, with the formation of miliary abscesses. No hard and fast line can be drawn between the severer forms of rheumatic endocarditis and ordinary septic thrombo-endocarditis. Differences may depend upon degrees of virulence of the invading bacteria.

Symptoms.—In the SIMPLE, BENIGN FORM, subjective symptoms, other than those of the primary infection with its fever and leukocytosis, may be slight or absent, or there may be oppression and pain in the precordial region with tachycardia and a sense of palpitation. Objectively, soft systolic murmurs are audible at the apex or, more rarely, over the aorta. There is usually accentuation of the pulmonic second sound. There is danger, in the acute stage, of embolism and of infarction (brain, heart, spleen, kidneys, intestine). There may be cyanosis of the face, arms and legs, associated with pallor due to anemia. The maximal and minimal blood pressures fall. The size of the heart often increases, owing to more or less dilatation. Pericarditis, myocarditis and pleuritis are common complications. In the rheumatic cases, the endocarditis may be associated with tonsillitis, polyarthritis, or chorea. There is nearly always a leukocytosis. Lesions in the parietal endocardium may lead to fibrosis and to conduction disturbances. Most cases of chronic inflammatory cardiopathy are sequels of acute endocarditis and acute myocarditis.

Fig. 276.—Erythema multiforme with Chorea, Mitral Insufficiency and Stenosis and Chronic Tonsillitis. (Med. Service, J. H. H.)

In the SEVERE, SEPTIC, ULCERATIVE FORM, the symptoms are usually more stormy at onset, though they may sometimes resemble those in the milder form. Usually, there is high fever, with joint pains, chills,

sweats, and outspoken polymorphonuclear leukocytosis and anemia. Tachycardia, palpitation, dyspnea, and prostration are prominent phenomena. Not infrequently, conjunctival, retinal, or subcutaneous hemorrhages occur, the latter often in petechial form. The urine contains albumin, casts, and, sometimes, blood. The spleen is usually palpable (acute splenic tumor). Murmurs (systolic or diastolic) become audible over the heart. Signs of acute circulatory insufficiency may be present, or the signs of myocardial insufficiency with dilatation of the heart gradually develop. As a result of septic emboli, the signs of infarction of the kidneys, spleen, intestine, brain, lungs, or heart may appear.

Clinically, several types are distinguishable (Osler): (1) *septic type*, with rigors, sweats, irregular fever and bacteriemia; (2) *typhoid type*, with more continuous fever, early prostration, delirium, diarrhea, drenching sweats and petechiae; the heart signs may be insignificant; (3) *cardiac type* of Bramwell, with the acute infection superimposed upon an old valve lesion; (4) *cerebral type*, simulating meningitis; (5) the *more chronic* or *subacute infective type*, resembling recurring malarial attacks extending over many months (6 to 13), in which there are fever, recurring chills, and progressive weakness. (See Endocarditis lenta).

Diagnosis.—The condition will be discovered, in the majority of cases, if the patient be carefully studied by physical and by laboratory methods. The fever, the tachycardia, the leukocytosis, the development of heart murmurs, and the presence of a primary focus of infection, are clews to diagnosis. The mildness or the severity of the symptoms and the course, but, more particularly, the character of the bacteria found in the blood by cultural methods, will help to distinguish the simple from the ulcerative form. In the cases resembling typhoid fever, the pulse rate, the leukocytosis, and the blood culture differentiate. In the cerebral type, the positive blood culture and the negative findings in the cerebrospinal fluid obtained by lumbar puncture will rule out meningitis. The blood culture is essential, and media of different kinds should be employed in order that the etiological agent may be discovered; the gonococcus, the influenza bacillus, and the rheumatic coccus of Rosenow are difficult to grow except on special media. It would be unfortunate, too, to miss the streptococcus viridans of endocarditis lenta, on account of the grave prognosis in the latter condition.

It should be remembered that the occurrence of "accide
in acute febrile infections may mislead, when no endo
Again, if an old valvular lesion be present, the murmur m
for that of acute endocarditis, if the previous condition
unknown. Not infrequently, however, an acute endoca
posed upon an old valvular lesion.

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(b) *Subacute Infective Endocarditis (Endocarditis lenta)*

Definition.—A subacute inflammation of the lining membrane of the heart, due to infection with the *Streptococcus viridans,* almost always terminating fatally after months of illness.

Pathology.—The portal of entry is often an infected tooth, or a pyorrhea alveolaris, though other portals may, in some instances, be responsible. Rigid, warty, masses develop on the heart valves, and there is a pronounced tendency for the process to extend to the mural endocardium; thus, when the mitral valve is attacked, the endocarditis often spreads to the posterior wall of the left atrium, and when the aortic valve is diseased, the process goes on to involve the endocardium of the wall of the left ventricle and the ventricular surface of the mitral cusps. At autopsy, the signs of embolic glomerulo-nephritis are almost always present (Baehr). Infarctions of various organs (brain, spleen, kidneys) are usually found.

Symptoms.—The patients have fever over a long period. They become anemic, sallow, develop petechial hemorrhages, and, sometimes, tender nodules in the skin of the hands and feet. The urine contains albumin and casts, and frequently blood, owing to the embolic glomerulo-nephritis that is nearly always associated. The temperature may become almost

normal for a time, only to recur later on. The duration is from 4 to 18 months, and the possibility of its existence should be thought of in long-continued fever, with chills, sweats, and leukocytosis, that is otherwise unexplained. The disease is almost uniformly fatal, though now and then a case recovers, as has been proven by Libman of New York, who has made a very careful study of the disease.

Diagnosis.—Failure to diagnose this disease is very common among general practitioners. Mistaken diagnoses of malaria, pulmonary tuberculosis, and subacute rheumatism are often made. Even when an endocarditis is recognized, its grave nature often goes unsuspected. And yet, as a rule, the diagnosis is relatively easy, if malaria and typhoid be ruled out by blood examinations, if a careful physical examination be made, if the leukocytes be counted, and especially if endocarditis lenta be thought of and a search made for the streptococcus viridans by suitable cultural methods in blood taken by syringe from a vein at the bend of the elbow. If the first blood culture be negative, others should follow at intervals; the streptococcus viridans will sooner or later be recovered, if endocarditis lenta exists. The patients may, for a long time, not seem to be very ill, and a consultant that makes the diagnosis often has a hard time in convincing the less-experienced practitioner that an exceedingly grave malady is before him.

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(*c*) *Chronic Endocarditis*

Definition.—A chronic inflammation of the lining membrane of the heart.

Etiology.—This probably always begins as acute endocarditis due to some bacterial infection. In many cases, after the acute process is over, a slow, more or less slumbering, inflammation continues, with occasional flare-ups (*endocarditis recurrens*), resulting gradually in fibrosis of the valves. Sometimes, the process is insidious from the start, especially in nephropathic or in tuberculous patients that become infected secondarily with streptococci of low virulence.

Symptoms.—The signs of valvular disease (*q. v.*) gradually develop.

Diagnosis.—When signs of a valvular lesion exist without fever, it may be hard to decide whether a chronic endocarditis is present, or whether one is dealing with an arrested process. A gradual increase of the signs of valvular involvement speaks for a continuance of the inflammatory process.

Atherosclerotic valvular lesions may simulate those due to chronic endocarditis; formerly, no distinction was made between them.

2. Myocarditis

Definition.—An inflammation of the musculature of the heart.

Etiology.—Two groups of cases are known: (1) myocarditis due to metastatic infection from some distant primary focus (tonsillitis, diphtheria, influenza, oral sepsis, etc.); and (2) myocarditis due to extension *per continuitatem* from an endocarditis or a pericarditis. In some instances, doubtless, the endocardium, the myocardium and the pericardium are simultaneously involved as a result of the bacteriemia.

Pathology.—Histologically, several varieties of inflammation of the myocardium are recognizable; clinically, it is difficult enough, as yet, to be sure that a myocarditis exists, let alone to differentiate the several varieties.

(a) Parenchymatous Form (*M. parenchymatosa*).—Very common in diphtheria; more rarely in typhoid and streptococcus infections. Hyaline and waxy degeneration of heart-muscle fibers; healing by minute scars. Occasionally, sudden death in acute stage.

(b) Purulent Form (*M. purulenta*).—Usually a complication of ulcerative endocarditis, due to infected emboli.

(c) Acute Interstitial Myocarditis (*M. interstitialis acuta*).—Minute foci

of primary proliferation of fixed tissue cells with aggregations of lymphocytes, plasma cells and eosinophils; degenerative changes in muscle fibers; healing by small scars (typhoid, streptococcus and other infections).

(d) Rheumatic Myocarditis (*M. rheumatica*).—Peculiar, submiliary nodules in interstitial tissue; cells with large nuclei, of connective-tissue origin; some lymphocytes and eosinophils. Sub-endocardial distribution of nodules, often destroying parts of conduction system.

(e) Tuberculous and Syphilitic Forms (*M. tuberculosa; M. syphilitica*).—Rare, though gummata of the septum occasionally cause heart block.

Symptoms.—The disease is nearly always a complication of some infection, especially of rheumatism, diphtheria, sepsis, typhoid, or scarlet fever. Fever, pressure or pain in the cardiac region; pallor or cyanosis, tachycardia or bradycardia, or arhythmia may suggest its development. The heart is often dilated. Systolic murmurs may be due to relative insufficiency or to a complicating endocarditis. In severe cases, the stasis phenomena of decompensation (albuminuria, edema, dyspnea, enlarged liver) appear. Death may occur suddenly (as in the children who fall over dead in convalescence from diphtheria), or gradually through progressive dilatation.

Mild cases recover in a few weeks or months with little or no residue; others go on to productive changes (*myocarditis chronica*) with scar formation, a form of chronic inflammatory cardiopathy, often spoken of as chronic fibrous myocarditis.

The *senile heart,* at autopsy, nearly always contains patches of fibrous change in the myocardium.

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3. Pericarditis

Definition.—An inflammation of the pericardium, or closed serous sac that surrounds the heart.

Etiology.—This is always due to bacterial infection; the fibrinous and serofibrinous forms are often due to the virus of rheumatic fever. The bacteria most often responsible are streptococci, staphylococci, pneumococci and tubercle bacilli.

The bacteria reach the pericardium: (a) through the lymph vessels (*lymphogenous form*), as a complication of pleuritis, subphrenic peritonitis, myocarditis, or mediastinitis; or more often (b) through the blood vessels (*hematogenous form*), as a metastatic infection complicating tonsillitis, typhoid or pyogenic infections of various sorts.

Chronic nephritis strongly predisposes the pericardium to infection. Tuberculous pericarditis is not uncommon, especially as a part of a polyserositis.

Classification and Pathology.—The acute forms are classified according to their exudates, since these give rise to different clinical symptoms.

1. Fibrinous or Dry Pericarditis (*Pericarditis fibrinosa s. sicca*) is the most common form. The fibrinous exudate may be very slight; when more abundant, it forms ridges or villi on the epicardium (cor villosum). On healing, the fibrin may be entirely absorbed, or it may undergo organization in places, leaving sclerotic patches on the surface of the heart. Sometimes, pericardial adhesions unite the visceral to the parietal layer. Occasionally, the whole pericardial cavity is obliterated (*total synechia* or *concretio pericardii*).

2. Pericarditis with Effusion (*Pericarditis exudativa*).—Here, the fibrinous exudate is accompanied by serous, hemorrhagic, purulent, or putrid effusion.

Symptoms.—In a sharp attack, the patient complains of violent pain in the region of the heart, shortness of breath, oppression, and a feeling of anxiety. Sometimes, however, the onset is insidious with weakness, headache, anorexia, and chilly sensations; in such cases, the patient may experience no pain in the region of the heart.

Dyspnea and cyanosis are nearly always present, even when there is no marked effusion. There is usually some fever and tachycardia; sometimes, the pulse is irregular. Over the heart, a pericardial friction rub (*q. v.*) may be palpable and audible (*pericarditis sicca*). If pericarditis be suspected, one should listen carefully, especially at the base of the heart, the patient being told to hold his breath after a full inspiration.

If a fluid exudate be poured out (*pericarditis exudativa*), the friction rub will disappear. The effusion leads to enfeeblement of the apex beat and to its displacement downward and to the left. The apex beat some-

times lies medial from the left margin of the area of cardiac dullness. The areas of cardiac dullness, both superficial and deep, are broadened, since the fluid tends to collect in the lateral regions of the pericardial sac. As the effusion grows, the areas of superficial and deep cardiac dullness coincide. One of the earliest signs of pericardial effusion is obliteration of the

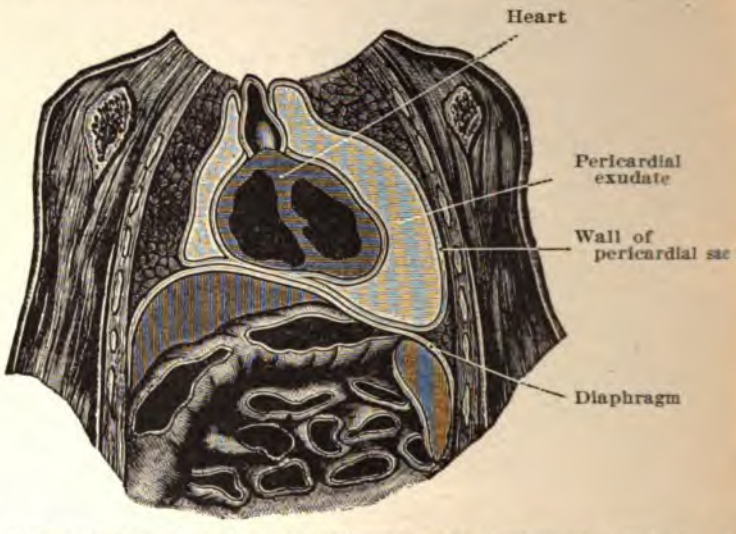

Fig. 277.—Frontal Section Through a Pericardial Exudate (Half Schematic), Showing the Pushing Down of the Left Side of the Diaphragm, the Position of the Heart and its Apex, and their Relation to the Right and Left Portions of the Exudate. (After Curschmann in J. Schwalbe's "Therap. Technik," published by G. Thieme, Leipzig.)

cardiohepatic angle; instead of being a right angle, it becomes very obtuse. When the effusion is large, a triangular area of dulness, a little rounded at the apex, can be made out; this corresponds to the equilateral triangular shadow seen on röntgenoscopy.

As the effusion accumulates, the left lung becomes compressed; dulness can be made out on percussion over the left lower lobe, enfeebled or bronchial breathing becomes audible under the angle of the left scapula and there is increased vocal fremitus.

Pericarditis may cause irritation of the neighboring nerves. Thus, irritation of the N. vagus or of the N. recurrens may lead to laryngeal paralyses or to dysphagia; irritation of the N. phrenicus may cause hiccough, paroxysmal eructations, or vomiting.

When a pericardial effusion occurs in young children, an outspoken heart-boss or *voussure* may develop. In adults, especially in those that suffer from emphysema, an effusion may cause a bulging in the epigastrium.

3. The signs of adherent pericardium (PERICARDITIS ADHAESIVA) include: (1) fixation of apex beat, (2) systolic retraction of the apex and of

the lower part of the sternum, (3) Broadbent's sign (*q. v.*), and (4) diastolic collapse of the veins of the neck. A pulsus paradoxus, in which the pulse becomes smaller, or actually disappears, during full inspiration, is occasionally present but is by no means constant.

The *diastolic shock* or *rebound* accompanying the second sound may be markedly exaggerated over the cardiac area in adherent pericardium (Broadbent); an intense shock may, in addition, accompany the protodiastolic third heart sound (W. S. Thayer).

Murmurs are often present, most often owing to associated valvular lesions. But even in the absence of valvular disease, a presystolic rumble may be audible, due perhaps to stretching of strands of adhesions when the atria contract.

When the pericardium is adherent to the diaphragm we may, on listening over the stomach, hear heart-sounds that are loud and metallic in quality (Reiss; François-Franck).

If, in adherent pericardium, the anamnesis be carefully gone into, it will often be possible to get a history of an earlier febrile attack accompanied by pains in the chest and palpitation.

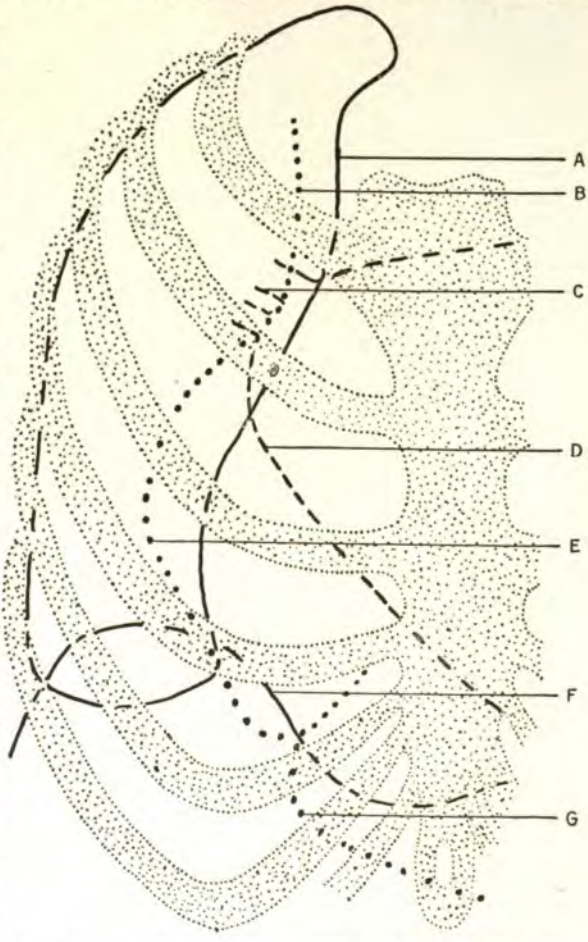

Fig. 278.—Diagram Showing Factors that May Affect the Cardiohepatic Angle (Continued). Displacement of the Lower Part of the Right Wall of the Pericardium, either by Effusion or Great Dilatation of Right Auricle, the Front Projection of the Organs in Mitral Stenosis is Shown. *A*, Anterior Medial Border of Right Lung; *B*, Right Wall of Superior Cava and Right Atrium; *C*, Pulmonic Veins; *D*, Right Wall of Left Atrium; *E*, Right Atrium; *F*, Diaphragm; *G*, Right Ventricle. (After W. J. Calvert, J. H. H. Bull.)

Adherent pericardium, if associated with mediastino-pericarditis, leads, sooner or later, to symptoms of chronic circulatory insufficiency

(cyanosis, dyspnea, cardiac arhythmia, stasis phenomena). Such symptoms are due to atrophy or degeneration of the myocardium and are to be regarded as danger signals. Unless the adhesions uniting the pericardial sac to the sternum be severed, the outlook is grave; but with Brauer's operation of cardiolysis, which Kocher calls "thoracolysis peri-

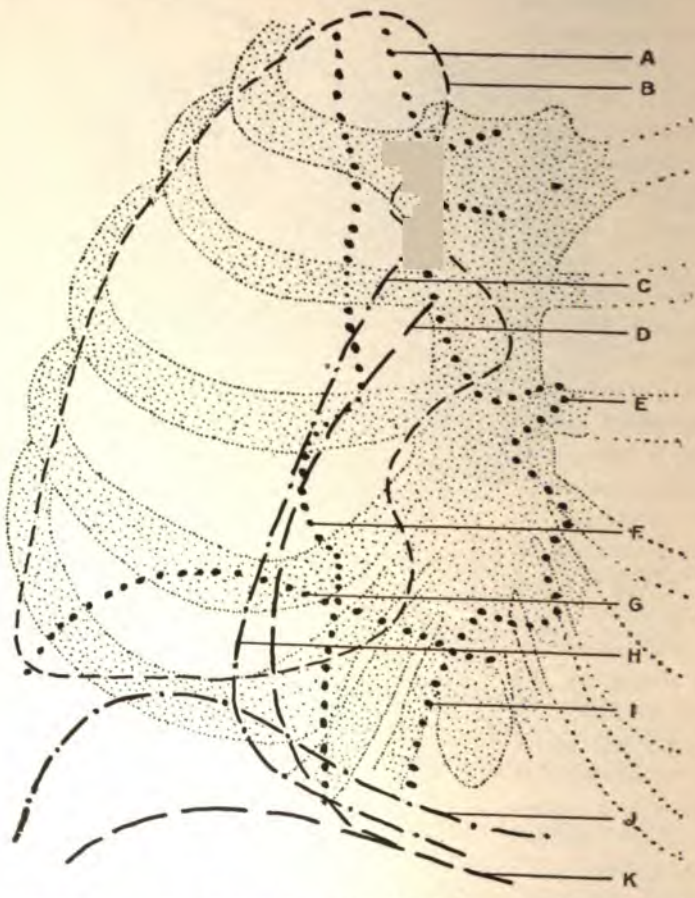

Fig. 278a.—Diagram Showing Factors that May Affect the Cardiohepatic Angle; Displacement of the Root of the Lung. The Front Projection of an Enlarged Heart in Aortic Stenosis is Shown, and also the Right Wall of the Pericardium and the Diaphragm in Two Cases of Pericarditis. *A*, Jugular Vein; *B*, Anterior Medial Border of Lung; *C*, Right Wall of Pericardium, with *J*, its Corresponding Diaphragm in Pericarditis; *E*, Left Wall of Right Atrium; *F*, Right Wall of Diaphragm of Heart Case; *H*, Lower Portion of Pericardial Wall in Displacement; *I*, Inferior Vena Cava. (After W. J. Calvert., J.

cardiaca," many of these patients can be rescued. have advised removing the sternum and its anterior p the posterior periosteum behind (König, Blauel), an o even better results

If mediastino-pericarditis exist, the abdomen should also be carefully examined, for the thoracic condition may be complicated by chronic productive perihepatitis (icing-liver) and ascites (Pick's syndrome). See Part VIII.

Fig. 279.—Case of Pericarditic Pseudocirrhosis. (After Cabot, from A. D. Hirschfelder's "Diseases of the Heart and Aorta," published by J. B. Lippincott Co., Philadelphia.)

Diagnosis. — Pericarditis will scarcely be overlooked, provided a careful physical examination be made. If effusion be present, paracentesis of the pericardium may be undertaken and the character of the fluid determined by bacteriodiagnostic and cytodiagnostic methods (See Exploratory Punctures).

Röntgenoscopy and röntgenography are valuable aids in the diagnosis of adherent pericardium (M. Benedikt; Stuertz; Lehmann and Schmall). The strands of adhesions are directly visible, though care must be taken not to be misled by shadows normally present in the lung areas near the pericardium. When in doubt, an examination should be made when the structures are rendered tense by a deep inspiration; in adherent pericardium, the margin of the sac will be pulled downward and outward by the strands of adhesions.

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E. Non-inflammatory Diseases of the Pericardium

Among those of chief clinical interest are: (1) hydropericardium, (2) hemopericardium, and (3) pneumopericardium.

Hydropericardium.—By this is meant a non-inflammatory accumulation of serum within the pericardial sac. It is due either to venous stasis, to a pathologically increased permeability of the blood vessels, or to both. It is met with in chronic circulatory insufficiency (in association with hydrothorax, ascites, and general anasarca), in chronic nephropathies, and in cachectic states (carcinoma, chronic tuberculosis). Clin-

ically, the signs of pleural effusion are present. On paracentesis, the fluid is found to be a transudate, not an inflammatory exudate.

Hemopericardium.—Blood may accumulate in the pericardial cavity as a result (1) of partial rupture into it of an aneurism of the heart, of the ascending aorta, or of the pulmonary artery; (2) of oozing in states of hemorrhagic diathesis; or (3) of trauma.

If the hemorrhage be large and occur quickly, the patient becomes dyspneic, cyanotic, and arhythmic, loses consciousness and dies. Should it be smaller, or occur slowly, the dyspnea and cyanosis are slower in developing, the area of cardiac dullness increases, and the heart sounds become distant. Paracentesis of the pericardium reveals blood.

Pneumopericardium.—An accumulation of air or of gas in the pericardial cavity may be due (1) to trauma in which the chest wall is perforated; (2) to rupture of a pneumothorax, of a lung cavity, or of a gastric or esophageal ulcer into the sac; or (3) to putrefactive decomposition of a pericardial exudate. The area of cardiac dullness is replaced by an area of resonance or of metallic tympany when the patient is in the recumbent posture; dullness may appear in the same area when the patient sits up. The heart sounds have an amphoric or a metallic quality. When liquid and air are both present, the water-wheel sound (*bruit de moulin*), may be heard, and, sometimes, if the patient be shaken, a Hippocratic succussion-splash may become audible. Pneumopericardium may resemble gaseous distention of the stomach or a partial pneumothorax near the heart, but röntgenoscopy and röntgenography will differentiate.

F. Valvular Diseases of the Heart

Definition.—By valvular disease of the heart is meant an interference with the function of the heart valves due to some organic disease of the heart.

When the valves close incompletely and allow blood to leak back through them, we speak of *regurgitation* or of *insufficiency of the valve;* when the valve-edges grow together, or when for any other reason an orifice is narrowed, we speak of *obstruction* or *stenosis* of the valve. Insufficiency of a valve will reveal itself during those phases of the cardiac revolution in which the orifice is normally closed; a stenosis, on the other hand, during those in which the orifice is normally open and a current passing through it. Sometimes insufficiency of a valve is combined with stenosis of the same valve, though, clinically, one or the other is usually the more prominent lesion.

Etiology.—Valvular insufficiency and valvular stenosis are usually *endocarditic* in origin, though changes in the aortic valve, and sometimes also in the mitral valve, may be *atherosclerotic* or *luetic*.

sufficiencies may be due also to widening of the orifices from relaxation of the muscle ring about the valve in myocardial weakness and in failure of tonicity (so-called *relative* or *muscular insufficiencies*), or they may follow changes in the papillary muscles (fatty degeneration, inflammation, fibrosis). Rarer forms of valvular defect are due to *congenital anomalies,* to *trauma,* or to *tumors.*

Effects of Valvular Disease.—In valvular disease, the normal mechanism of the heart is disturbed, in that the portion of the heart "down-stream" from the diseased valve receives less blood than normal, whereas the portion of the heart "up-stream" gets more. The latter then attempts to "compensate" for the disturbance; in valvular insufficiency, it will send forward a larger amount of blood than normal at each beat, whereas in valvular stenosis an effort is made to force the blood through the narrowed orifice with increased force. The insufficiency will thus lead to *hypertrophy together with dilatation,* stenosis (at first) to *hypertrophy* alone. As long as the heart muscle is able to adapt itself to these disturbed conditions, the heart is in the stage of *compensation.* Sooner or later the heart becomes unequal to the task and there is failure of compensation (*decompensation*).

The heart muscle has, normally, remarkable POWERS OF ADAPTATION to the variable demands made upon the heart for work. The heart can vary (1) its *systolic output* and (2) its *frequency of contraction;* on these two factors, the amount of blood pumped into the aorta each minute, the so-called *minute-volume,* depends.

It is asserted that simply in walking on the level the heart has to do four times as much work as when the person is at rest, and that when the body is exerting itself to the utmost the heart does 13 times the amount at rest (Zuntz). No wonder then that the heart muscle, confronted by a valvular defect that throws more work upon it, can easily and quickly adapt itself to the new conditions as long as the heart muscle itself remains uninjured. The increased work calling continuously upon the reserve force of the heart causes HYPERTROPHY of the musculature of its walls. In animal experiments, the volume and weight of the muscle may be demonstrably increased within a month after a valvular lesion has been produced. The individual muscle fibres enlarge and there is also an increase in the number of heart-muscle cells. For a long time it was thought that such hypertrophied hearts have less reserve force than the normal heart, but recent studies indicate that the reserve forces of the hypertrophic and of the normal heart are equal in amount.

The increased diastolic filling of the heart in each cardiac cycle accounts for the increased systolic output; such a DILATATION of the heart is necessary as a compensatory process, and is spoken of, sometimes, as a *physiological* or *compensatory dilatation.* But in larger valve defects, and when the heart muscle is weakened, the increased diastolic filling is not perma-

nently compensated for by increased systolic output and then a *pathological dilatation* occurs, known also as *systolic dilatation,* or *stasis dilatation.* In such cases, the intramuscular connective tissue is stimulated to proliferation and *myofibrosis cordis* develops.

Sooner, or later, the adaptive powers of the heart begin to fail and symptoms of DECOMPENSATION begin to appear. This may result from (1) an *extension of the valvular injury* (endocarditis recurrens, mesaortitis luetica, atherosclerosis), but more often decompensation sets in because of (2) *degenerative processes in the heart muscle,* due to prolonged overwork, to intoxications, or to infections.

Decompensation may be manifested in the *pulmonary circuit* by stasis phenomena in the lungs (heart failure cells in the sputum or a tendency to chronic bronchitis; later, infarction of the lungs, or pulmonary edema).

Decompensation in the *systemic circulation* may reveal itself by cyanosis, dyspnea and signs of chronic passive congestion in the organs (tender palpable liver; scanty, dark, albuminous urine; ascites; right-sided hydrothorax), by edema of the ankles, or by the occurrence of embolic infarctions (brain, spleen, kidneys). These phenomena have already been discussed under Chronic Circulatory Insufficiency.

Frequency of Defects of the Several Valves.—Hirschfelder has analyzed 1,781 cases of valvular disease of the heart studied in the medical clinic at the Johns Hopkins Hospital (1899-1908), and found the following incidence:

Mitral insufficiency	29 per cent.
Aortic insufficiency	22 "
Mitral stenosis and aortic insufficiency	14 "
Mitral stenosis alone	8 "
Aortic and mitral insufficiency with mitral stenosis	4 "
Aortic insufficiency and aortic stenosis	3 "
Other valvular defects	20 "

Külbs, in a collective review, estimates the incidence of the several valvular diseases as follows:

Mitral insufficiency	20-40 per cent.
Mitral insufficiency and mitral stenosis	6-33 "
Aortic insufficiency	10-22 "
Mitral stenosis alone	5-21 "
Aortic insufficiency and mitral stenosis	3-14 "
Aortic and mitral insufficiency	
Other valvular lesions	

Age.—In the *first decade* of life, the valvular lesio
all congenital; in the *second* and *third* decades, the
ditic, and, indeed, largely rheumatic in origin and
lesions; in the *third* and *fourth decades* occur the ma

involving chiefly the aortic valves; and in *later life* (after the 40th year) the atherosclerotic lesions, involving the aortic valve or the aortic and mitral together, predominate.

Recognition.—The existence of valvular disease is recognized largely by means of auscultation, though percussion and x-ray examinations help to reveal the changes in the various cavities of the heart that result from the processes of accommodation and of compensation of the lesion. In the *stage of compensation,* an exact diagnosis is usually easily made; after the *stage of decompensation* has set in, there may be more difficulty, owing to the complications arising from muscular insufficiencies and the modifications of the auscultatory signs resulting from the enfeeblement of the heart muscle.

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1. Aortic Stenosis

Narrowing at the aortic orifice gives the left ventricle more work to do when it empties itself; hence hypertrophy of its walls, with only moderate dilatation follows. The right ventricle becomes an appendage to the left, the wall of the latter bulging into the former.

The apex beat is slightly displaced downward and to the left, and is not markedly increased in strength; there is very little enlargement of the heart to the left until dilatation occurs. A loud systolic murmur is audible in the aortic area; it is propagated especially toward the vessels of the neck. A palpable systolic thrill is demonstrable in the second right intercostal space. The second sound in the aortic area is feeble or absent. The pulse is small, prolonged, and anacrotic; bradycardia is common.

Orthodiagrams and electrocardiograms point to hypertrophy of the left ventricle. Syncopal attacks are common.

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2. Aortic Insufficiency

Some blood regurgitates from the aorta into the left ventricle during diastole. Since, in diastole, the ventricle also receives its normal amount from the left atrium, its cavity dilates. At each systole, a larger amount of blood is thrown into the aorta and the wall of the left ventricle hypertrophies.

The apex beat is forcible, resistant, circumscribed (*choc en dome*), displaced markedly to the left and often downward to the sixth intercostal space. The areas of cardiac dullness are enlarged to the left and upward. A horizontal position of the heart with dynamic dilatation of the aorta (large systolic output) can be made out on röntgenoscopic examination. The electrocardiogram also points to hypertrophy of the left ventricle. A characteristic blowing murmur, soft, aspirative, commencing with the beginning of diastole and replacing the sound due to closure of the aortic valves, or following immediately upon this, can be heard; this murmur is sometimes short, occupying only a part of the long pause, but ordinarily it is long and decrescendo in character, lasting through diastole; it is audible in the course of the blood current giving rise to it, *i. e.*, in the aortic area, along the left margin of the sternum, as far as the xiphoid; occasionally, it is maximal at the apex, and, rarely, it can be heard in the axilla and along the left margin of the heart (Rufus Cole.) Occasionally, the murmur is musical, especially when the insufficiency is due to rupture of a valve, or to atherosclerosis. The murmur is sometimes scarcely audible at all, or it may be heard only when the patient sits, or stands, or takes exercise; it is sometimes heard better with the naked ear than with the stethoscope. A systolic murmur at the apex, due to relative mitral insufficiency, is frequently associated with it. The first sound at the apex is often indistinct. Occasionally, a presystolic murmur near the apex can be heard; this is the "Flint murmu
ficiency." Other phenomena pointing to aortic insufficie
pulsus celer or Corrigan pulse, throbbing of carotids, to
Duroziez's double murmur in the peripheral arteries; p
and a capillary pulse.

Many of the cases of aortic insufficiency are due
(Wassermann reaction); many to atherosclerosis; som

If the Wassermann reaction be positive, especial pains should be taken to ascertain if an aneurism coexist.

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3. Mitral Stenosis

The mitral orifice is obstructed and too little blood flows from the left atrium into the left ventricle in ventricular diastole and, consequently, into the aorta in ventricular systole. Hypertrophy and dilatation of the left atrium develop; increased pressure in the pulmonary circulation, and hypertrophy of the right ventricle are results of the effort to overcome this. Later, the right ventricle dilates, when it becomes insufficient for the work required of it. In pure mitral stenosis, the left ventricle atrophies and becomes an appendage of the right ventricle.

The apex beat is feeble unless the apex is formed by the right ventricle, when it may be stronger. Visible rotary or wavelike pulsation can be seen in the precordium. There is enlargement of the area of cardiac dullness to the right, and Krönig's "steplike line" bounding the area of superficial cardiac dullness on the right, can be made out. A chimney-shaped area

of dullness along the left sternal margin is due to the dilated pulmonary artery and the enlarged left atrium. Relative dullness over the left atrium may be demonstrable in the left interscapular space. Mitral configuration of the heart is characteristic on x-ray examination. Epigastric pulsation due to the hypertrophied right ventricle is common. A diastolic rumble, a presystolic murmur, or both, can be heard at the apex, often accompanied by palpable thrill in the apex region. The first sound at the apex is a loud snap, with corresponding abrupt palpable shock (*dureté clôturale*); the pulmonary second sound is strongly accentuated. Double, or split, second sounds are audible at the base and sometimes, at the apex. The pulse is small, soft, and often irregular. There is a high *P*-wave on the electrocardiogram when the atrium is hypertrophied and active.

In both mitral stenosis and mitral insufficiency, the patients may exhibit a "high color" in the cheeks and slight cyanosis of the lips (*mitral facies*).

Most important in making the diagnosis are (1) the palpable thrill and the rumble, in diastole, (2) the snapping first sound, (3) the accentuated and split second sound in the pulmonary area. In the late stages, a pulsus irregularis perpetuus, due to atrial fibrillation, is common. Embolism is a very common complication in mitral stenosis.

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4. Mitral Insufficiency

During systole, part of the blood from the left ventricle regurgitates through the insufficient mitral valve into the left atrium; hence, dilatation of the left atrium occurs and there is increased pressure in the pulmonary circulation, which, in turn, leads to hypertrophy (and later to dilatation) of the right ventricle and accentuation of the pulmonary second sound. An increased amount of blood passes from the dilated left atrium, during diastole, into the left ventricle, and leads to dilatation of the latter. The left ventricle, pumping out larger amounts of blood than normal, hypertrophies.

The apex beat is forcible and diffuse; it is displaced somewhat lateralward. The areas of cardiac dullness are enlarged to the left and, in severe cases, also to the right. A chimney-shaped area of dullness may be demonstrable near the sternum in the second intercostal space. Mitral configuration of the heart is visible on x-ray examination. A systolic murmur of blowing quality is audible; it is maximal at the apex, often replacing the first sound there. This murmur is decrescendo in character, usually holosystolic, and is propagated toward the axilla and the angle of the scapula in the back. The pulmonary second sound is accentuated. The pulse is of normal volume and tension in the stage of compensation, becoming small and irregular when decompensation sets in. Symptoms of chronic passive congestion of the lungs are common; there is a tendency to bronchitis and the sputum contains cells filled with brown pigment ("heart-failure cells"). There may be dyspnea on slight exertion, and cyanosis, even when the heart is fairly-well compensated. The distinction between mitral insufficiency due to valvulitis and that due to muscular relaxation has been referred to above (see Heart Murmurs).

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5. Pulmonary Stenosis

This is a rare lesion, usually congenital, and then often combined with other anomalies in so-called "blue babies" (*morbus caeruleus*). There is hypertrophy and, later, dilatation of the right ventricle. A systolic murmur is audible; it is maximal in the pulmonary area, and is accompanied by a palpable thrill. The pulmonary second sound is feeble or absent. Dyspnea is present on exertion. The child has Hippocratic fingers.

scopy, marked systolic dilatation of the second of the three curves on the left margin of the cardiovascular stripe can be seen. A systolic thrill and a systolic murmur are demonstrable over the pulmonary area.

Patent interventricular septum and **patent foramen ovale,** are defects that rarely occur singly, and the diagnosis may be difficult to establish *intra vitam.* In *defect of the interventricular septum,* a loud, rough, high-pitched systolic murmur, often obscuring the two heart sounds, is audible at the level of the third left intercostal space, or at the level of the fourth chondrosternal articulation, on the same side (Roger); it is sometimes audible in the whole precordial region. It is propagated in a transverse direction —never toward the left clavicle —a fact that distinguishes it from the murmur of pulmonary stenosis. The murmur begins with systole and is audible during both of the normal sounds of the heart. A thrill may, or may not, accompany it. Hypertrophy and dilatation of the right heart occur.

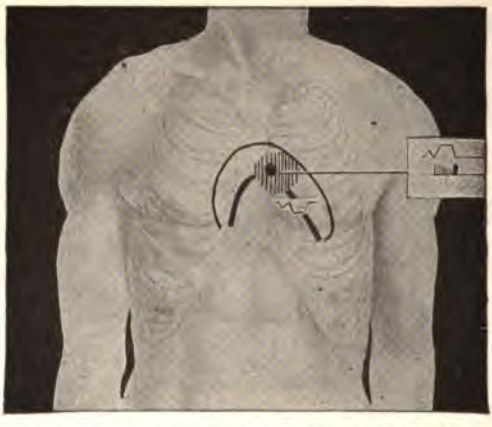

Fig. 280.—Distribution and Character of the Murmur Due to a Patent Interventricular Septum (Roger's Murmur). (From A. D. Hirschfelder's "Diseases of the Heart and Aorta," published by J. B. Lippincott Co., Philadelphia.)

Patent foramen ovale may yield no physical signs as long as the pressure relations in the two atria are normal. When the pressure rises in either atrium, blood will flow through the orifice and may produce murmurs (systolic, diastolic, or both). Occasionally, paradoxical embolism occurs; by this is meant transport of thrombi from the body veins directly into the general arterial circulation. Another peculiarity is the occurrence of a "ventricular type" of jugular phlebogram in mitral insufficiency associated with patent foramen ovale; it is due to regurgitation of blood from the left ventricle into the left atrium, and, thence, through the foramen ovale into the right atrium, the vena cava superior and the jugular vein.

Stenosis of the Isthmus of the Aorta.—This anomaly is usually easily recognizable, from

(1) Signs of dilatation of aorta (dullness in the right intercostal space; high pulsation of the aorta in ju tive insufficiency, with marked dilatation and hypertrophy triele);

(2) Marked dilatation and visible pulsation of upper half of body, with small, delayed pulse in the v half of the body;

(3) Collateral circulation between the upper half and the lower half of the body in the form of visible, tortuous, pulsating, superficial arteries on the trunk (there may be a systolic thrill and a murmur in these).

Transposition of the Heart (Situs inversus cordis).—Congenital dextrocardia is usually a part of a general situs viscerum inversus. The apex-beat is in the fifth intercostal space between the right parasternal and mammillary lines. The areas of cardiac dullness, and the cardiovascular stripe on x-ray examination, present a mirror picture of the normal relations. The electrocardiogram is characteristic.

Ectopia cordis.—As a congenital anomaly the heart may be so displaced as to lie no longer within the thorax. Thus it may lie (1) high up in the neck (*cervical heart*), (2) on the front of the chest, when there is fissure of the sternum (*pectoral heart*), or (3) in the abdominal cavity, when the diaphragm is defective (*abdominal heart*).

Fig. 281.—Ectopia cordis Secondary to Malformation of the Sternum—Pectoral Heart. (After G. Fay, "Arch. des Maladies du cœur," published by Baillière et Fils, Paris.)

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H. The Chronic Toxic-degenerative Cardiopathies

Under valvular diseases and chronic myocarditis, above described, are included the chronic cardiopathies of inflammatory origin (*cardiopathia chronica inflammatoria*). In contrast with these are the chronic cardiopathies that are degenerative or circulatory, and not inflammatory, in origin (*cardiopathia chronica degenerativa s. circulatoria*). This group includes:

(1) The atherosclerotic cardiopathy (*C. atherosc*
(2) The fatty cardiopathy or heart of obesity (*C.*
(3) The nephropathic cardiopathy (*C. nephropath*
(4) The thyreotoxic cardiopathy (*C. thyreotoxica*

In these different forms of myodegeneratio cordis, toward the end, to see an atrial fibrillation, with pu[illegible] [illegible] develop

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1. The Atherosclerotic Cardiopathy (Cardiopathia atherosclerotica)

This may depend (a) partly upon increased resistance to the arterial flow due to the sclerosis of the peripheral vessels and to the arterial hypertension often accompanying it, leading especially to hypertrophy of the left ventricle; (b) upon sclerosis of the coronary arteries, leading to secondary thrombosis of their smaller branches with necrosis of the heart muscle, and, later, scarring; (c) upon atherosclerosis of the aortic and mitral valves and of the annulus fibrosus, the sclerosis and calcification of these valves and of the fibrous ring leading to stenoses and insufficiencies.

Atherosclerotic cardiopathies rarely become noticeable before the fortieth year. The predisposing causes include potatorium, syphilis, lead-poisoning and physical overexertion. The early hypertrophy gives way, later, to dilatation and to all the signs of myocardial, or chronic circulatory, insufficiency. Marked bradycardia, cardiac asthma and stenocardiac attacks (angina pectoris) are suggestive of the atherosclerotic heart and particularly of the form due to coronary sclerosis. Sudden death often follows upon thrombosis or embolism of one of the larger coronary vessels.

The His bundle is frequently involved in the atherosclerotic cardiopathy, the lesions revealing themselves by delay of conduction (or by partial or complete heart block) and the Morgagni-Adams-Stokes syndrome.

2. The Fatty Cardiopathy or Heart of Obesity (Cardiopathia adipositatis)

This is due to a marked proliferation of the epicardial adipose tissue and a growth of fatty tissue between the muscle fibers of the myocardium, especially in the conus of the right ventricle. The injury to the heart is probably due less to the local fatty infiltration than to the demands made by the general obesity of the body upon a heart relatively too small to meet them.

The obesity is usually complicated also by myodegeneratio cordis and by atherosclerotic lesions.

The hypertrophy and dilatation of the heart are best made out on x-ray examination, since obesity interferes with satisfactory percussion and localization of the apex beat. Dyspnea on exertion, cardiac asthma, stenocardiac and syncopal attacks are common. The blood pressure is often elevated, especially in patients with associated arteriolar sclerosis.

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3. The Nephropathic Cardiopathy (Cardiopathia nephropathicorum)

(Traube's Heart)

The nephropathic cardiopathies are most marked in patients that suffer from contracted kidneys with continuous arterial hypertension. In addition to the hypertension as a cause of the heart hypertrophy, direct toxic factors have to be considered, since the hypertrophy affects the whole heart and not merely the left ventricle. Hypertrophy of the adrenal medulla has been pointed out recently as an accompaniment of the heart hypertrophy in contracted kidney and it has been suggested that an increased secretion of epinephrin may explain the arterial hypertension. The proof has, however, yet to be brought. The permanent vasoconstriction tends soon to be accompanied by general atherosclerosis, which, in turn, hastens the development of myocardial insufficiency. The signs of decompensation of the heart begin with dyspnea, malleolar edema and ur

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4. The Thyreotoxic Cardiopathy (Cardiopathia thyreotoxica)

There is every transition from the mild tachycardia of slight grades of hyperthyroidism to the grave cardiopathies with hypertrophy, dilatation and ultimate asystole of the severer cases. In every unexplained tachycardia, hyperthyroidism and thyreo-intoxication should be kept in mind as a possible cause. Whether the thyreotoxic substances act directly upon the heart muscle, or chiefly upon the nervous system (stimulation of the accelerators) is not known. The diagnosis is usually easy. (See Graves's Disease and Thyreotoxicosis). Atrial fibrillation may be a late phenomenon.

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5. Other Forms of Chronic Cardiopathy

Under this designation are included the chronic degenerative cardiopathies due to various infections and intoxications. Many of the cases described clinically as "chronic myocarditis" or "idiopathic heart-hypertrophy" are really instances of toxic degeneration of the heart muscle. The whole group of chronic cardiopathies depends upon injury to the cardiac muscle, the noxa causing degeneration of the muscle fibers, scar formation, hypertrophy of the remaining fibers and, finally, failure of tonicity. In each patient studied, the effort should be made to ascertain the various mechanical, infectious and toxic factors that may have been responsible for the injury to the heart muscle. Small foci of chronic infection (*e. g.*, oral sepsis, infected paranasal sinuses, chronic prostatitis) have to be considered here, just as when studying chronic polyarthritis.

J. Angina pectoris

(*Stenocardiac Attacks*)

Definition.—An affection in which, on slight exertion, paroxysms of retrosternal or, less often, precordial pain occur, sometimes extending into the left arm, accompanied by a sense of constriction due to contraction of the intercostal muscles, and by characteristic mental anxiety or a sense of impending death.

Nature.—The pathogenesis is not wholly clear. In most cases, there is sclerosis of the coronary arteries or a luetic lesion at the root of the aorta. In the *angina that follows exertion,* the cause is most often a narrowing of the coronary arteries (*stenocardia*); in the *angina pectoris of decubitus,* the cause is usually an acute dilatation of the heart.

Etiology.—The causes of atherosclerosis and of lues must be looked upon as the causes of the lesions that underlie angina pectoris. It is believed that tobacco, alcohol, tea and coffee, in excess, may be important contributing factors. Gout, obesity, and infections predispose.

In patients over 45, the commonest cause of angina pectoris is atherosclerosis; in younger people, the condition is most often due to aortitis associated with lues, rheumatism or influenza.

Symptoms.—A sudden pain is felt in the region of the heart, behind the sternum, or in the epigastrium; it rapidly increases in violence and may be so severe as scarcely to be bearable. It is rather vaguely localized, is cramplike in character, and often extends down the medial side of the left arm to the elbow, wrist, and little finger. It is accompanied by great anxiety, by a pinched look to the face, and a grayish pallor, sometimes by lachrymation and sweating. The patient stands stock-still when attacked and anxiously awaits the passing of the attack. The duration is from a few minutes to a half-hour or longer. The attacks nearly always follow

Fig. 282.—The Shaded Area Shows the Distribution of the Cutaneous Hyperalgesia. After the First Attack of Angina pectoris. (After J. Mackenzie, "Symptoms and Their Interpretation," published by Shaw & Son, London.)

Fig. 283.—After Repeated Attacks of Angina pectoris the Pain and Hyperalgesia Extended to the Regions Shaded Here. Note the Area in the Neck and Medial Side of Right Elbow. Compa Illustration. (After toms and Their Inte by Shaw & Son, Lond

exertion, though this may be slight. Many patients ca without an attack. Walking after a meal, or against a especially likely to excite an attack. Sometimes the ir on the heart by digestion will provoke a paroxysm

Abortive attacks occur; some of these are so slight that no actual pain is experienced (*angina sine dolore*). The blood pressure of patients who suffer from angina is often low; it may rise 30-60 mm. in an attack, or may not change at all. Physical examination of the heart may reveal no abnormalities.

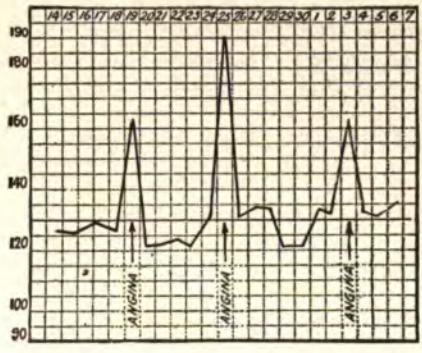

Fig. 284.—Blood Pressure Curve Showing Crises of Hypertension During Attacks of Angina pectoris. (From A. D. Hirschfelder's "Diseases of the Heart and Aorta," published by J. B. Lippincott Co., Philadelphia.)

Differential Diagnosis. — The most common error is to look upon a paroxysm of angina pectoris as an attack of "acute indigestion." Attempts are often made to distinguish true angina (*angina vera*) from false angina (*angina spuria*). Certain it is that the attacks of *angina vasomotoria* that occur in Graves's disease, and the attacks of *angina nervosa* that occur in young women, have a different significance and gravity than the attacks of angina pectoris associated with lesions of the aorta and of the coronary arteries. The aorta should be examined röntgenologically in cases of angina pectoris.

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K. Diseases of the Arteries

Certain disturbances of development have been referred to above under diseases of the heart. The most important arterial diseases met with clinically are: (1) atherosclerosis; (2) syphilitic arteriitis; (3) thrombosis and embolism; (4) aneurisms; (5) thromboangeitis obliterans; and (6) periarteriitis nodosa.

1. Atherosclerosis, or Arteriosclerosis

Definition.—A primary degeneration (atheroma nodules, chiefly in the intima and partly in the media), with secondary sclerotic connective-tissue formation; a progressive disease, the commonest and most varied lesion in the vascular system.

Pathology.—The disease is rare before middle life, but juvenile arteriosclerosis occurs. The distribution of the lesions is extremely variable (local or general). The process may affect the aorta chiefly, or the peripheral arterial system chiefly, or it may be limited alm
arterial domains (atherosclerosis or the cerebral a
arteries, of the renal arteries, of the mesenteric
arteries).

The relation of the degenerative process to th
vary greatly. When the former predominates, the
weakened, undergo diffuse dilatation, and are sub

tial ruptures (*e. g.,* of the cerebral arteries). The degenerative process may reach the lumen and break through (*atheromatous ulcer*); the contents of an ulcer may be swept off as emboli, or may become the seat of platelet- and fibrin-deposits (*thrombosis*). An atheromatous ulcer may rupture externally (*hemorrhage*), or blood may become extravasated between the arterial walls (*dissecting aneurism*), especially in the aorta and larger arteries.

When the sclerotic process predominates over the atheromatous, the course may be more benign, though gradually, through alteration of the general conditions of the circulation leading to changes in the velocity of the blood flow and often to arterial hypertension, great strain is thrown upon the heart and large vessels.

In the smaller vessels, the sclerotic process may take the form of an obliterating endarteritis. This, combined with calcifications of the media and thrombosis in the lumina of the small vessels, may cause: (1) gangrene in the extremities; (2) cerebral softening; (3) myomalacia cordis, with rupture of the heart; or (4) fatal degenerations of the heart muscle (coronary sclerosis).

Etiology.—The process has been supposed to be due chiefly to chronic intoxications (alcohol, lead, gout, diabetes, syphilis and other infectious diseases, nephritis, adrenal hypertrophy, digestive disturbances). Certainly, such intoxications may play a part. As one's clinical experience grows, however, one is more and more impressed with the importance of the quality of tubing a person starts with, and the character of his endocrine glands.

Diagnosis.—(1) General Peripheral Arteriosclerosis.—The radial, brachial, temporal and crural arteries are accessible to palpation. The arteries roll under the fingers; hardening and thickening of the walls is

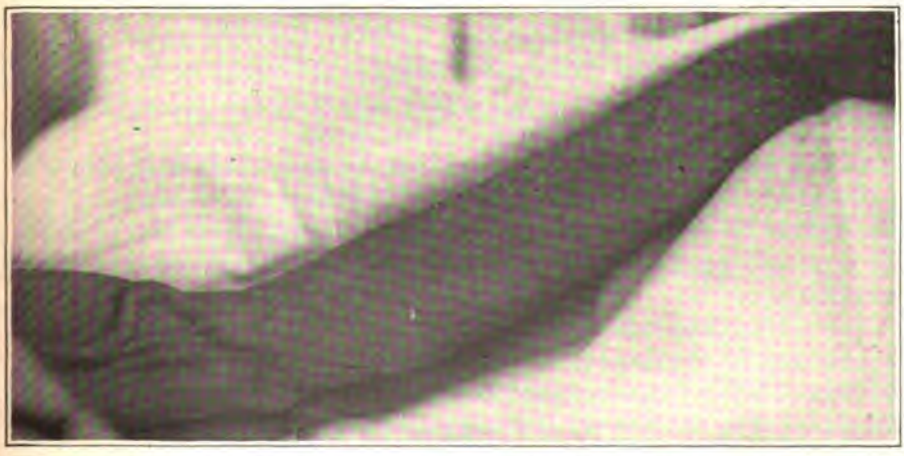

Fig. 285.—Marked Peripheral Arteriosclerosis; Brachial Artery. (Med. Service, J. H. H.)

easily felt; the arteries are elongated and tortuous; a calcified radial may have a "goose-neck" feel. X-ray examinations will reveal the calcified arteries as shadows. The blood pressure is sometimes increased; but not always.

(2) Aortic Sclerosis or Central Sclerosis.—This may occur even when the peripheral arteries are unaffected. The patients may complain of a burning feeling behind the sternum and of anginal symptoms. Physical examination reveals retrosternal dullness; a dilated aorta is visible on x-ray examination; there is a ringing aortic second sound; sometimes, aortic insufficiency develops and, occasionally, aortic aneurism.

The most common form of sclerosis of the aorta is one in which the atheromatous lesions are most marked at the level of the abdominal aorta. In this portion, the normal intima may be almost entirely replaced by atheromatous ulcers and calcified atheromatous plaques while, higher up, at the level of the aortic arch, only a few, early, smooth, yellow nodules are to be seen. The condition is not usually discoverable clinically. In other cases, the upper portion of the aorta may be extensively involved.

(3) Sclerosis of Arteries Supplying Special Domains.—Atherosclerosis in the smaller arteries supplying individual organs disturbs their nutrition and may give rise to important symptoms.

(*a*) *Cerebral Atherosclerosis.*—This is common after the sixtieth year. The patients complain of headache, of an indescribable "numb feeling" in the head, of vertigo and of depression. After a time, cerebral apoplexy, or softening due to thrombosis, causes paralysis, aphasia, apraxia, etc. Ophthalmoscopy reveals retinal atherosclerosis. Mental reduction is common (*atherosclerotic dementia*). See Part XII.

(*b*) *Coronary Sclerosis.*—This has been referred to under diseases of the heart (*q. v.*).

(*c*) *Renal Atherosclerosis.*—This leads to the atherosclerotic contracted kidney when the larger renal vessels are involved, or to hypertensive nephropathy when the small arterioles are diffusely involved (see Part X).

(*d*) *Atherosclerosis of the Mesenteric Vessels.*—This may give rise to attacks of violent colic with meteorism (*dyspraxia intermittens atherosclerotica or angina abdominis*). If the vessels supplying the pancreas are involved, pancreatic atrophy may result (diabetes, or pancreatic hemorrhage).

(*e*) *Atherosclerosis of the Arteries of the*
patients may be comfortable when resting, but fee
walking. They begin to limp and soon have to sit
tent claudication of Charcot; *dysbasia intermitten*
The foot becomes pale in the attack and the puls
The symptoms are probably due to a tonic spasm

(*vascular crises* of Pal). If the lumen of a peripheral artery be completely obliterated, gangrene results (senile gangrene, diabetic gangrene, etc.).

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2. Syphilis of the Arteries (Arteriitis syphilitica)

The most important of the infectious diseases of the blood vessels is syphilis. The veins and lymph vessels may be affected in all stages of the disease; syphilitic arteriitis is most common in tertiary lues, though it may occur within six months after infection. The arteries at the base of the brain are especially predisposed to involvement, and the adjacent arachnoid is nearly always simultaneously diseased (distinguished from atherosclerosis).

The ascending aorta is very frequently involved **(mesaortitis productiva syphilitica)**. There is frequent involvement of the orifices of the coronary arteries, with angina pectoris. Aneurismal dilatation of the aorta is common between the thirty-fifth and the forty-fifth years of life. Symptoms of aortic syphilis resemble those of atherosclerosis of the aorta, but they appear earlier in life, though often years after the external symptoms of syphilis have disappeared. The Wassermann reaction is usually positive, and is a great help in recognition.

Patients with syphilis, especially with congenital syphilis, show a definite tendency to early general atherosclerosis of a non-specific type. The radials feel like rubber tubes. In any young person showing general arteriosclerosis, syphilis as an etiological factor should be strongly suspected. (Nonne.)

True syphilitic arteriitis, as at present recognized, is less widely generalized. It is usually seen as a process localized in the aorta or in the cerebral vessels; very often, it may be active in both situations in the same patient.

In the smaller arteries, infiltration about the vasa vasorum, in the media (*mesarteritis*), and in the adventitia (*periarteritis*), leads to disturbances of nutrition of the vessel wall. A compensatory proliferation of the intima occurs (*obliterative endarteritis*); and complete occlusion of the vessel by thrombosis is the usual end-result.

In larger arteries, especially in the aorta, an infiltration of the media and adventitia occurs in circumscribed patches in the wall. Destruction of muscle-fibers and elastic tissue is found in such areas, with substitution of granulation tissue (*mesaortitis productiva*). The media undergoes compensatory proliferation. As retraction of the granulation tissue in the media occurs, the intima is drawn down. It is this process that gives these patches of syphilitic aortitis their characteristic wrinkled or puckered appearance. The destructive processes in the media result in thinning and weakening of the vessel wall; the ultimate result of this is a general dilatation of the vessel, or, in some cases, the production of a true aneurism.

In both smaller and larger vessels, the infiltrative process may assume the form of true gummatous nodules. The Treponema has been demonstrated in these lesions.

Syphilis of the Aorta.—Syphilitic aortitis (Heller-Döhle) shows a marked tendency to localization at the root of the aorta, in contradistinction to the usual aortic atherosclerosis, which is chiefly developed in the aorta descendens (Mönkeberg). It is most common in the later stages of syphilis. It is not usually discovered clinically until, by its extension, complications are produced, the symptoms of which are more obvious. Such, in order of frequency, are: (1) involvement of the aortic valves (aortic insufficiency) (*q. v.*), (2) aneurism formation, (3) extension to the coronary arteries (stenocardiac attacks).

It is important to recognize aortic syphilis earlier, before the occurrence of these complications. It should be looked for in every case of syphilis of more than a few months' standing. The dilatation of the ascending aorta can often be suspected from the presence of retro- and parasternal dullness at the level of the first to the third interspace. The röntgenoscopic examination gives more definite information. It is often combined with some hypertrophy of the left heart even before any valvular lesion can be discovered. A moderate hypertension is common. This condition, in a patient below 45 and without nephritis, should in itself be considered very suspicious of vascular syphilis. A history of luetic infection, or a positive Wassermann, are valuable for confirmation. Babinski states that in cases of syphilitic aortitis the slowing of the heart that is a normal reflex response to pressure on the eyeballs is absent. Serological or clinical evidence of coincident luetic cerebral endarteritis is present in a high percentage of cases of syphilitic aortitis.

Syphilis of Cerebral Arteries.—Two chief forms are descril
endarteritis of the larger arteries of the base of the brain leads to partial or complete obliteration of the vessel lumen with res or softening of corresponding portions of the brain. Hemiplegia are the common clinical results. (In some cases, the diseased ve an apoplexy occurs.) At times, however, aneurism formation oc of one of these cerebral arteries. Such luetic aneurisms are large as opposed to the numerous miliary aneurisms on atheros symptoms are those of cerebral tumor.

Nissl and Alzheimer's endarteritis of the smaller vessels of the brain is believed by these authors to be the commonest cause of syphilitic epilepsy.

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3. Aneurisms

Definition.—An aneurism is a chronic dilatation of the lumen of an artery with new formation of the wall, thus differing from mere ectasia of an artery (dilatation through stretching of an atrophic wall) and from an intra- or extramural hematoma (communication of the lumen of the artery with another blood cavity through a ruptured wall).

Varieties.—An aneurism may be circumscribed or diffuse. *Circumscribed aneurisms* may be saccular, circular, boat-shaped or funnel-shaped. The *diffuse aneurisms* may be spindle-shaped or cylindrical.

A *dissecting aneurism* develops through the rupture of the inner and middle coats and the spread of the blood for long distances between them and the outer coat of the vessel; it would be better described as an *intramural hematoma.*

Sites.—An aneurism may occur in any artery in the body. It is most common in the ascending aorta and in the aortic arch. Popliteal aneurisms are common. In the viscera, aneurisms are not uncommon in the cerebral, pulmonary, and splenic arteries. They are more rarely found in the mesenteric and the coronary arteries. The so-called miliary aneurisms on the cerebral arteries are not true aneurisms but are small hemorrhages into the arterial sheaths. In the peculiar disease known as *periarteritis nodosa* (*q. v.*) a very large number of aneurisms of the small arteries are met with. The nature of this disease is obscure.

Size.—An aneurism may be microscopic in size, or, in the aorta, may be as large as a child's head. (Fig. 287.)

Walls.—The wall of the aneurism always shows a br
the coats of the artery. In circumscribed aneurisms, t
margin of the dilatation. In diffuse aneurisms there ar
intercalated among islands of fairly-normal lamellated w
the elastic lamellae predominantly, but the connective tissu
also interrupted. As a rule, the intima breaks first, then the

adventitia. The lacunae due to the breaks are filled up in all aneurisms with new connective tissue. Owing to the changes in the wall, this yields to the blood pressure, which causes a bulging. If new connective tissue be formed in sufficient amounts, rupture may be long postponed. Most aneurisms are progressive, though in rare instances they become stationary.

Fig. 286. — Treponema pallidum from the Wall of an Aneurism. (After Wright and Richardson, in A. D. Hirschfelder's "Diseases of the Heart and Aorta," published by J. B. Lippincott Co.)

Etiology.—The causes are manifold (trauma, atherosclerosis, gummatous syphilitic arteritis, and other infectious forms of arteritis). Lues is by far the most common cause of aneurism of the aorta. (Fig. 286.)

Complications.—Aneurisms may invade neighboring organs (adhesions, erosions, compressions), and may finally rupture externally, or into a body cavity or a canal. Rupture into a vein causes *varicose aneurism.*

(*a*) *Aneurism of the Thoracic Aorta*

The most common cause is syphilis. Most cases of aortic aneurism are to be looked upon as complications of a preëxisting syphilitic aortitis by which the wall of the aorta has been weakened (*vide supra*). These aneurisms are frequently fusiform, but clinically the most common form is the saccular. The symptoms and signs of aortic aneurism vary markedly with the site of the aneurism, in the ascending, transverse, or descending portions of the arch of the aorta or in the descending aorta.

In cases of ANEURISM OF THE ASCENDING PORTION OF THE ARCH the

Fig. 287.—Unusually Large Aortic Aneurism. Photographed the Day Before Death. (After W. H. Hough, J. H. H. Bull.)

physical signs are usually more prominent than the symptoms. The aneurism tends to grow into the right pleural cavity reaching the chest wall usually in the second or third interspace where pulsation is early to be made out on inspection. On palpation, this pulsation is felt to be expansile in character. A thrill and diastolic shock are often felt over this area. A loud aortic second sound is heard on auscultation. An aortic systolic murmur is common and a diastolic murmur is present when the aortic valves have been involved by the luetic process. An abnormal area of dullness is made out above and usually somewhat to the right of the cardiac dullness. The left border of the heart is usually forced to the left of the mammillary line. The chief symptom associated with this type of aneurism is the pain resulting usually from pressure on, and erosion of, the anterior chest wall. In time, a large tumor, projecting from the chest wall, may result from such erosion. Anginal pain may likewise result from involvement of the orifices of the coronaries. Pressure on the superior vena cava may cause engorgement of the vessels of the head and arms. Hoarseness may be caused by injury to the right recurrent laryngeal nerve.

In ANEURISM OF THE TRANSVERSE AND DESCENDING ARCH of the aorta symptoms arising from pressure are more prominent than physical signs. Small aneurisms in this location may cause symptoms by pressure, when yielding no signs on palpation, percussion, or auscultation. They tend to grow posteriorly, but may point against the anterior chest wall in the midline or to the right of the sternum. In some cases, they form pulsatile tumors, posteriorly, in the left interscapular region. Involvement of the large arteries given off from the arch may cause inequality in the radial pulses, due to retardation, or diminished volume, on one side. A distinct pulsatile downward jerk may be transmitted to the trachea (*tracheal tug*). Pressure on the sympathetic may lead to inequality of the pupils. The commoner symptoms are cough (often brassy in character), bronchorrhea, and fever, due to compression of a bronchus (usually the left); hoarseness, or aphonia, due to pressure on the left recurrent laryngeal nerve; pain due to erosion of the vertebrae, or of the posterior or anterior chest wall; dysphagia, from pressure on the esophagus.

ANEURISMS OF THE DESCENDING THORACIC AORTA are often latent. They may give rise to pressure effects; pain due to erosion of the vertebrae (often, when involving the nerve roots, this pressure causes intercostal neuralgia); dysphagia; symptoms and signs of pulmonary compression.

(*b*) *Diagnosis of Aortic Aneurism*

It should be suspected and looked for in every pa
syphilis, especially when oppression in the chest, inte
hoarseness, or difficulty in swallowing are complained
any suspicion of the existence of an aortic aneurism, a

examination (röntgenoscopy) should be made. If an aortic aneurism exists, an abnormal, dark, pulsating shadow will be recognized. The borders of the shadow are sharply circumscribed. The expansile pulsation, if seen in two different spots of the same shadow, can be regarded as pathognomonic. The röntgenoscopic examination should be made not only in the sagittal direction, but also with oblique transillumination. With röntgenography, a permanent record may be made. (Figs. 288 and 289.)

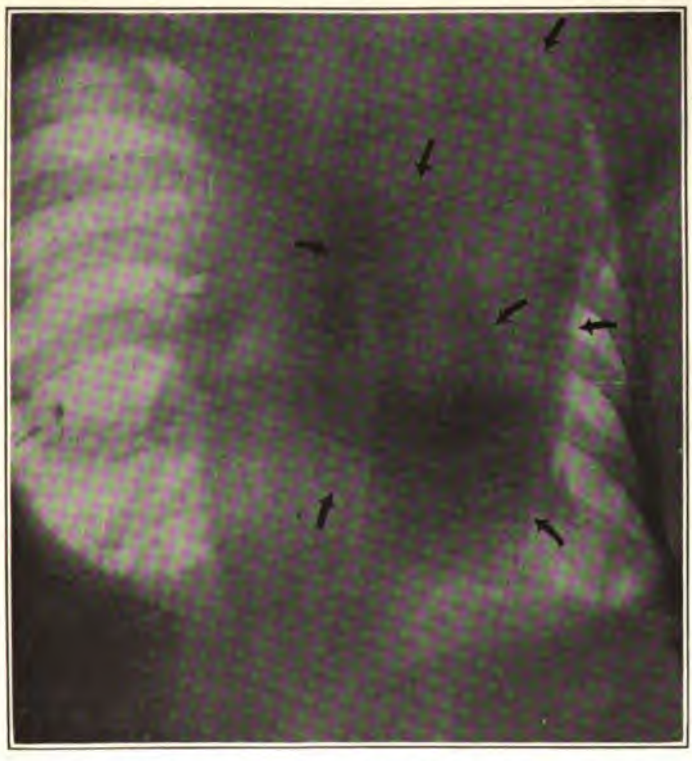

Fig. 288.—Large Thoracic Aneurism. Outline is Indicated by Outer Set of Arrows; Wire in Sac Indicated by Inner Set of Arrows. (X-ray Dept., J. H. H.)

Physical Signs.—Visible pulsation is met with in the first, second or third right or left intercostal space; on palpation, pulsation may be expansile and accompanied by thrill and by diastolic shock. If adherent to the trachea, a distinct *tracheal tug* may be felt when the fingers are pressed under the cricoid when the patient sits up with his head thrown slightly backward (Oliver-Cardarelli sign). Among the other important signs are dilatation of the superficial veins of the chest or in front of one shoulder, dislocation of the trachea, inequality of the pupils, paralysis of left N. recurrens (hoarseness, brassy cough, laryngoscopic examination), dyspnea, dysphagia, and inequality of the two radial pulses. A systolic murmur,

sometimes also a diastolic, may be audible over the aneurism. The left ventricle is not hypertrophied in aneurism, unless there be accompanying aortic insufficiency or other special cause.

Fig. 289.—Aneurism of Descending Portion of Arch of Aorta. (X-ray Dept., J. H. H.)

(*c*) *Aneurism of the Abdominal Aorta*

These aneurisms are rare in comparison with those of the thoracic aorta. The commonest site of occurrence is in the epigastric region. Gastric symptoms, especially vomiting, are frequent. More characteristic are severe neuralgic pains in the back, often radiating to the legs. Paraplegia may occur. In these cases erosion of the vertebrae has occurred. Large retroperitoneal masses may be formed by infiltration of the tissues. In these masses, which are largely composed of laminated clot honeycombed with blood spaces, little or no pulsation may be evident. The diagnosis is less difficult where a definite saccular tumor with expansile pulsation can be isolated, on palpation. Thrills and murmurs, both systolic and diastolic, may be made out over such tumors. The throbbing abdominal aorta, often found in neurasthenia, should not lead to errors in diagnosis, since the pulsation can be traced the length of the aorta and no localized tumor is present.

(*d*) *Diagnosis of Aneurisms of the Pulmonary Artery*

The mass may cause bulging, pulsation, systolic thrill and dullness in the second and third left intercostal space and behind the sternum. A

systolic murmur is audible. The signs are similar to those yielded by aneurism of the aorta. The murmurs of aortic aneurism are, however, propagated into the carotid arteries; those of pulmonary aneurism are not. Moreover, aneurism of the pulmonary artery does not affect the radial or the femoral pulse.

(e) *Arteriovenous Aneurisms*

In these cases, an abnormal communication exists between an artery and a vein. The etiological factor is usually trauma. The condition is accordingly found most often in the extremities. Rupture of an aneurism of the ascending portion of the arch of the aorta into the superior vena cava has been observed in a number of cases. There is cyanosis of the upper half of the body and, often, edema in the same area. In such cases, too, the ventricular type of jugular phlebogram is seen. Pulsation, marked venous engorgement, palpable thrill, and a continuous loud murmur with systolic intensifications, are characteristic of all cases of arteriovenous aneurism.

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4. Thrombosis and Embolism

Thrombi or emboli lead to occlusion of vessels and anemia (when end-arteries, necrosis) of the parts they supply. Thus arise *infarctions* of the lung, heart, brain, spleen, kidney and intestine (see these organs).

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5. Thromboangeitis obliterans

Definition.—A condition in which parietal, red thrombi occur in the blood vessels, especially in the arteries of the lower extremities, though the veins may also be involved.

Incidence.—The process is much more common in males than in females. It is a disease of middle life, and is especially common in Jewish people. For full description, see the papers of Leo Buerger of New York.

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6. Periarteritis nodosa

Definition.—A disease characterized by inflammatory infiltrations and fibrinous deposits beginning in the media and adventitia of the medium-sized arteries (especially the coronaries and mesenteric); minute aneurisms are for
thrombosed; sometimes, marked proliferation of the intima als

Etiology.—This is not yet clear, though lues and other i
have been held responsible.

Symptoms.—These vary according to the arter
affected, since the blood supply is partly cut off in
tribution of the diseased vessels. Among the symp

hemorrhage from the intestines and kidneys, cerebral hemorrhage, paralysis, muscular pains, and severe anemias. The disease is fatal in a few weeks, though a patient may, sometimes, recover after vigorous antiluetic treatment.

There is outspoken tachycardia, but no fever. When palpable vessels are involved, the nodules may be felt in their course.

Diagnosis.—This can only occasionally be made during life, when the symptoms above described are prominent and nodules are palpable on the peripheral arteries.

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L. Diseases of the Veins

1. Phlebitis and Thrombophlebitis

Definition.—An inflammation of the walls of the veins, often leading to thrombosis.

Etiology.—Nearly always, the disease is due to bacterial infection (streptococci). Infection may occur by direct extension, or it may be hematogenous or lymphogenous in origin. A peculiar luetic phlebitis is also described (B. Hoffmann).

Symptoms.—In the superficial veins, there is redness in the skin over the vein, and a tender cord is palpable where the deep veins are involved. The symptoms are vague at first (burning, formication, itching); later, intense boring pains may develop. Swelling and redness of the neighboring tissues appear. The danger of embolism is great, unless the part be kept at rest.

Thromboses may form and may extend into the larger veins, even to the vena cava.

Thrombophlebitis is common after childbirth (phlegmasia alba dolens) and in typhoid fever. There is a form of *recurring thrombophlebitis* that occurs in women, attacking, successively, the veins in different parts of the body; it is a grave malady.

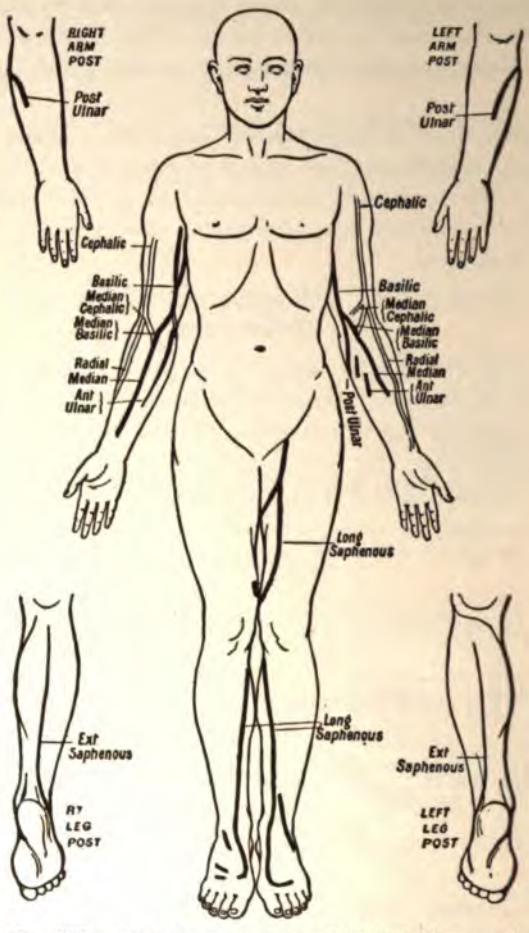

Fig. 290.—Diagram of a Case of Latent Cancer of the Stomach with Multiple Thrombi in the Veins. (After W. Osler and T. McCrae, "Cancer of the Stomach," published by P. Blakiston's Sons Co., Philadelphia.)

2. Varicose Veins

.—Varix is a pathological dilatation of a vein.

—Mechanical factors, obstructing the venous flow, are usuall
Varicose veins of the legs may be due to wearing
e on the veins within the abdomen (pregnancy, t
s requiring long standing. Varicose veins of the
the formation of a collateral circulation after portal
s hepatis).

s.—In the legs, the enlarged and tortuous veins
ellings, and they may be painful, especially on

ing. Pigmentations and atrophy of the skin accompany them, and often "varicose ulcers."

Varicosities of the hemorrhoidal veins are known as *piles* or *hemorrhoids.* They may cause great discomfort (itching, pain, hemorrhage). In esophageal varix, profuse hemorrhage is not uncommon and may first lead one to suspect a cirrhosis of the liver. (See Part VIII.)

3. Phlebosclerosis

The walls of the veins are sometimes palpably thickened, a process akin to atherosclerosis. The condition is, as yet, of but little clinical importance.

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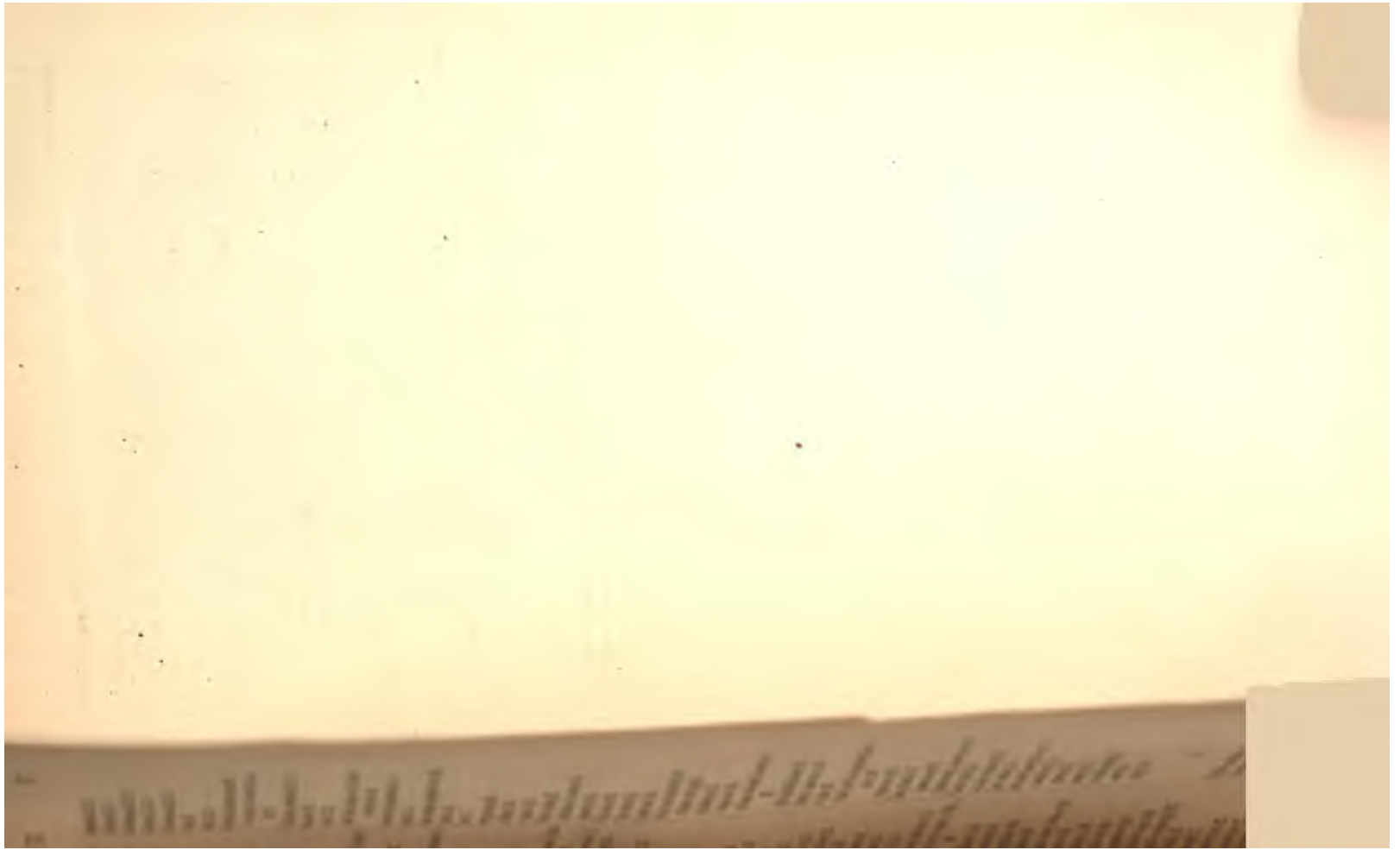

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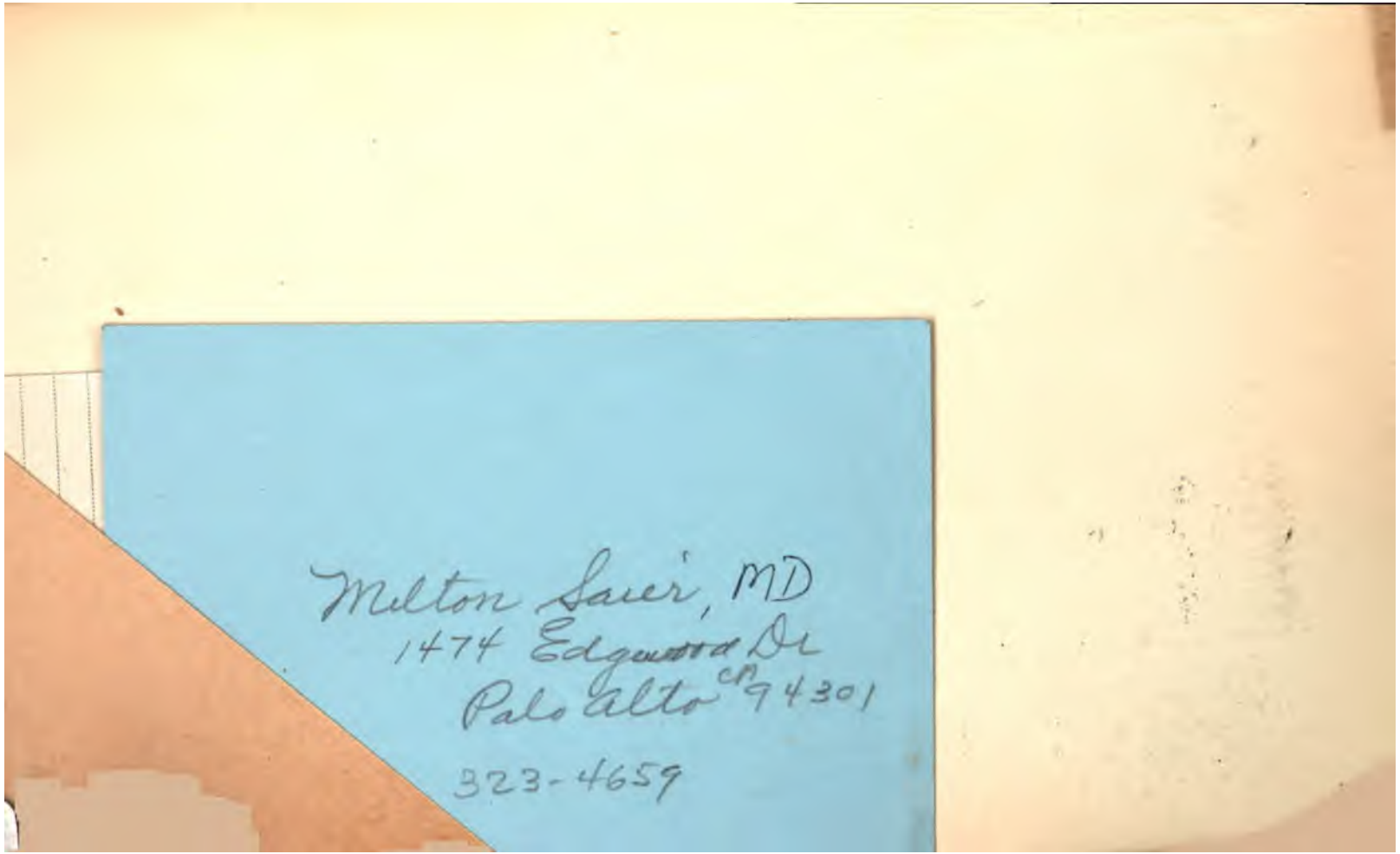
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